BUREAU OF HYGIENE AND TROPICAL DISEASES

BULLETIN OF HYGIENE

Volume 34, No. 4 April, 1959

Public Health

MINISTRY OF HEALTH. **Report of the Ministry of Health for the Year ended 31st December, 1957. Part I. 1. The National Health Service (including a Chapter on International Health). 2. Welfare, Food and Drugs, Civil Defence.** Cmnd. 495. pp. xvii + 254. 1958. London: H.M. Stationery Office. [12s.]

The main differences between this report and that for 1956 [this *Bulletin*, 1958, v. 33, 425] are that it contains a new chapter on the "Report of the Royal Commission on Mental Health", that it has 13 more pages and that it was submitted in July instead of October which is a welcome reduction in the time-lag.

It is the annual directors' report to the shareholders and, as such, is of interest to all who help to pay for the service as well as to those who work in it and those who use it.

Finance. The total cost of the National Health Service in the financial year 1956–7 was £585m., an increase of £50m. on the previous year. The main sources of the money were: £468m. from the Exchequer, an increase of £45m. and now 80% of the total cost; £37m. from the National Insurance Fund; £28m. from payments made by users of the service; £28m. from superannuation contributions and transfer values and £24m. from rates for their moiety of the cost of the local health authority services. The Hospital and Specialist Service cost £334m., an increase of £29m.: the General Medical Services, £58m., increase £3m.; Pharmaceutical Service, £60m., increase £8m.; General Dental Service, £40m., increase £4m.; and Local Health Authority Services, £50m., increase £4m. Capital expenditure for hospital development amounted to £12,845,563. Though still inadequate it is some improvement on the previous year and is to be increased to £17,771,000 in 1957–8.

Royal Commission on Mental Health. An outline of the report is given [this *Bulletin*, 1957, v. 32, 961] and close consideration is promised.

Hospitals. The number of available staffed beds remains unchanged at 477,000. The average number of occupied beds has declined steadily year by year from 428,000 in 1954 to 420,000 in 1957. The number of patients treated is going up owing to shorter average length of stay but the waiting lists are growing again after a satisfactory reduction in the previous year. Tables show the variations in the waiting lists between the different regions and the different departments. The longest is for the Ear, Nose and Throat departments, 1,491·8 per 100 beds in non-teaching hospitals and 1,803·8 in provincial teaching hospitals. The shortest is for chest diseases, 2·3 in non-teaching hospitals.

Psychiatric Services. The number of patients resident in mental hospitals at the end of 1957 was 143,220 (145,593 a year earlier) of whom 37% were "voluntary". The number of admissions is rising but the discharges exceed the admissions. The "Worthing Experiment" based on Graylingwell Hospital is described.

Much is being done to enlighten the public about mental illness and mental deficiency.

Tuberculosis. The average number of occupied beds was 20,085 compared with 24,478 in 1956 and 30,442 in 1953.

The Chronic Sick. Better use of existing rather than more beds is needed supplemented by better domiciliary and welfare services.

Staff. At the end of the year there were 6,902 consultants in the service, an increase of 163 during the year. Whole-time nurses and student nurses numbered 138,677 an increase of 1,758.

Other Hospital Matters. These include recruitment of nurses, administrative staff and student radiographers; the Hospital Organization and Methods Service; hospital costings; hospitals for war pensioners; the Polish hospital and the artificial limb and appliance service.

General Medical Service. The number of principals providing unrestricted general medical service increased by 212 to 19,507 of whom 12,962 practised in partnerships. In addition there were 1,465 assistants and 788 principals with restricted practices such as for hospital staffs only. The average number of patients per doctor shows, at 2,273, little change. During the year 1,763 practitioners attended official refresher courses.

General Dental Services. The demand for treatment was 5·2% greater than in 1956. The contribution paid by patients towards the £40m. which the service cost was about £8,156,000.

Drugs. The number of prescriptions dispensed was 207,209,397, the lowest since 1949 but the cost per

prescription continues to rise and 74% of the bill for drugs was for proprietary preparations.

The Local Health Authority Services. The number of domiciliary confinements attended by midwives was 255,747, an increase of 8,104. Attendances at all types of local authority clinics have increased. There were 10,176 home nurses and 6,293 health visitors on general duties and the domestic help scheme continues to expand. Up to the end of 1957 903,120 persons had been vaccinated with BCG under local authority arrangements. The number vaccinated against smallpox increased to 424,267 and another 113,843 were revaccinated. 546,776 children were immunized against diphtheria and 1,222,136 against poliomyelitis. More occupation and training centres for the mentally defective are being provided. There is much activity, which is described, in the health education field.

Miscellaneous. The chapter on medical and hospital supplies shows the gradual development of central purchasing, standardization and research. During the year there was considerable unease about the rates of pay of various grades of staff in the National Health Service and the various steps taken to deal with it are described. A reciprocal agreement has been reached under which British nationals, including tourists, in Sweden and Norway have the benefits of their national health service. The problems of the elderly, the handicapped and the homeless are dealt with in a special section. The Welfare foods service, Food and Drugs and Civil Defence are all well described.

There are the usual tables.

Few seeking information on the administrative or statistical sides of the National Health Service will fail to find what they need in this veritable encyclopaedia on the service. *Allen Daley*

ELLER, C. H., HATCHER, G. H. & BUELL, B. **Health and Welfare Issues in Community Planning for the Problem of Indigent Disability.** *Amer. J. Pub. Health.* 1958, Nov., v. 48, No. 11, Pt. 2, 1–49.

In the introduction to this paper there is some account of the work and aims of Community Research Associates, Inc., which, in 1947, undertook "a comprehensive synthesis of materials from the health, welfare, and recreation fields, relevant to over-all community planning". The investigations reported here were a direct outgrowth of this research and formed 1 of 3 local studies or projects. In Winona County, Minn., the project was focussed on dependency, in San Mateo County, Calif., on the problem of disordered behaviour and in Washington County (Hagerstown), Md., the project was primarily concerned with indigent disability. It is the last of these projects which is described at length in this paper. The information collected in 3 years is described, analysed and set out in 6 sections, 39 tables and an appendix on methods and procedures. The sections, each of which has a number of sub-sections, are entitled (1) objectives, concepts and principal methods, (2) the community programme, (3) the community problem of indigent disability, (4) treatment recommendations and implementation, (5) rehabilitation potentialities and treatment results and (6) programme implications.

[There is so great a mass of information, local detail and discussion in this report that a summary cannot do justice to the work.] *M. E. Delafield*

WELLIN, E. **Implications of Local Culture for Public Health.** *Human Organization.* 1958, v. 16, No. 4, 16–18. [15 refs.]

"Local culture has three sorts of broad implications for public health. First, it affects the objective profile, or the ecology, of health and disease. Secondly, it creates its own, or subjective, picture of health and disease. Finally, it influences the careers of health programs."

An instance of the first implication is the relationship between kwashiorkor and traditions of feeding and pregnancy in many countries at the present time. An example of the second implication is drawn from the fact that the Aymara people of Peru make no distinction between typhus and typhoid because, although they see the differences, they do so through a cultural screen which emphasizes the similarities (fever) and suppresses the dissimilarities.

The third implication involves 2 fundamental questions: (1) how does the community perceive and respond to the health programme, and (2) how do health workers perceive and respond to the community and its culture?

The important fact is that cultural patterns do influence health, and these patterns should be understood and taken into account; anthropology and medicine are strongly related. *Charles Wilcocks*

FLECK, A. C., Jr. & IANNI, F.A.J. **Epidemiology and Anthropology: Some Suggested Affinities in Theory and Method.** *Human Organization.* 1958, v. 16, No. 4, 38–40.

In this paper the author recalls the attitude of mind of men like BAKER who in 1767 identified lead poisoning as the cause of colic in cider-drinkers of Devonshire, Oliver Wendell HOLMES in Boston who in 1847 associated child-bed fever with certain obstetrical practices, and John SNOW who associated cholera with water supply in London in 1854. These men did not possess any previous knowledge which guided their thoughts, but by making careful studies of the total environment and activities of the communities concerned they were able to arrive at valid conclusions.

The moral is that the epidemiologist must recognize the importance of socio-cultural factors in the causation of disease, and this is as important now as it ever was—in tuberculosis work, for instance.

Charles Wilcocks

Maternal and Child Health

SYLVESTER, P. K. **The Changes in an Open Air School over Thirty Years.** *Med. Officer.* 1958, Sept. 19, v. 100, No. 12, 194–8, 2 figs.

This is the story of the gradual evolution of the functions of an open air school in the City of Oxford. It is probably typical of what is happening elsewhere in medium sized towns.

The paper traces briefly the history of day open air schools in England and Wales since the first was established by the London County Council in 1907. There have been 2 major changes. The first is the modification of the original spartan conditions particularly by the provision of some heating as advocated by the Ministry of Education in its report of 1949–50. The second is the provision in newly erected ordinary schools of better ventilation including a whole side of a class room being openable: "most modern school buildings provide an environment that is as good [as], if not better, than that provided at most open air schools".

The Oxford school opened in 1928 and was intended for 40 "delicate and nervous" children aged 8 to 11 in winter and 50 in summer. It came up to expectation specially for "the nervous, highly-strung child who would not eat and could not sleep".

From 1945 the medical conditions for admission were expanded and now there is a wide range including bronchiectasis, congenital heart disease, spina bifida, muscular dystrophy and residual palsy after poliomyelitis: 3 can get about only in a wheelchair. The age range is now 5 to 16. The number of "delicate" children is decreasing and the total number of children of all types in the school is now 32.

The children need more attention and a nursery-trained assistant has now been appointed to help the 2 teachers.

A remedial gymnast and the school doctor visit weekly. *Allen Daley*

Care of Old Persons and the Chronically Ill

ROTH, M. **Some Problems of Mental Health in Old Age.** *Roy. Soc. Promotion Health J.* 1958, Nov.–Dec., v. 78, No. 6, 813–22. Discussion 822–3.

In this report of an address given at a Sessional Meeting of the Royal Society of Health, the speaker first referred to the background of the changing incidence of diseases in the last 100 years, which has led to a lesser mortality among the lower age groups, but little reduction in the mortality among the older age groups, and he then spoke of the altered position of the aged in society. These facts, together with the increased number of admissions to mental hospitals, has encouraged greater prominence to be given to mental health in old age. One of the recent triumphs of medicine he states to be the demonstration that much illness formerly attributed to aging is, in fact, due to disease.

It is stressed that mental illnesses do not form a homogeneous entity due to cerebro-vascular degeneration, and in consequence a specific diagnosis must be made in each case and treatment and rehabilitation planned accordingly; and again, that mental and somatic conditions are so closely interrelated that any distinction made between them is both spurious and dangerous.

Social isolation is an existing factor in all forms of mental disease among the aged. This is admitted to be a vague expression, but suggestions for the protection of mental health include non-segregation of the aged in Town Planning, reconsideration of the retirement age, and a closer coordination of the domiciliary services concerned in the care of the aged.

Finally the idea has developed that the aged lose status in any country enjoying rapid social progress, which they themselves tend to accept, and the social and economic accompaniments produce in many spheres a real inferiority.

In the discussion the following among other points were touched upon:

(a) the corruption of Christian culture by materialism leads to the abandonment of parents to the care of the authorities;
(b) the importance of the aged sharing their interests with younger persons
(c) the need for intensive research into the process of aging itself. *C. O. S. Blyth Brooke*

FARQUHAR, R. W. **Care of the Aged: some Socio-Medical Problems.** *Roy. Soc. Promotion Health J.* 1958, Nov.–Dec., v. 78, No. 6, 824–31. Discussion 832–3.

This paper, given on the same occasion as the previous one, embodies an analysis of various circumstances of the 195 residents in the 5 hostels and former Public Assistance Institute provided for old persons in one of the Divisions of the Lancashire County Council.

The most interesting finding was that the primary reason for admission was the loss of former accommodation in 34% of the cases; the strain on relatives in 27%; loss of relatives or friends in 7%; being found

alone and neglected in 16%, and finding that they could no longer maintain themselves, even with the maximum help available, in the remaining 16%.

Reference was also made to the opening in May 1957 of a hostel to provide temporary accommodation both for the relief of those caring for the aged at home and to provide for holidays for them by the sea.

An important comment that is in line with experience elsewhere, is made in the conclusions, namely that many old people whose income is a little above the limit set for assistance from the State, appear to be at a great disadvantage in gaining admission to hostels.

Another important point made in the discussion was that many old people go into residential accommodation because they have not learned how to retire.

C. O. S. Blyth Brooke

Vital Statistics and Epidemiology

GABRIEL, K. R. & RONEN, Ilana. **Estimates of Mortality from Infant Mortality Rates.** *Population Studies.* 1958, Nov., v. 12, No. 2, 164–9.

The Population Branch of the United Nations Department of Social Affairs have proposed a scheme for constructing model life tables for undeveloped countries based on infant mortality in order that the expectation of life at birth and mortality rates at other ages can be estimated. The authors have examined the reliability of this method and found that an appreciable bias in the estimated expectation of life would make its use misleading. The authors attempted to improve on the United Nations method and although their method produced a much smaller bias they concluded that infant mortality alone was not likely to produce estimates that were of practical importance.

[In countries where registration of births and deaths is defective the estimation of infant mortality is difficult since the available data often only relate to small selected areas or to a particular group. In these cases it seems most unlikely that the estimated infant mortality is representative of the country as a whole or that it could be used for estimating other rates.]

W. J. Martin

ABHAYARATNE, O. E. R. **Infant Mortality in Ceylon.** *Ceylon Med. J.* (n.s.) 1958, May, v. 4, No. 3, 129–50, 11 figs.

The infant mortality in Ceylon is one of the highest in the world; for the first 45 years of the century it ranged between 120 and 263 deaths per 1,000 living births. The rate fell in 1946 and has continued to fall slowly. In the 21 registration districts of Ceylon the infant mortality in 1955 varied from 50 to 117. The division of the Island into 3 zones based on the rainfall during the south-west monsoon showed that there was a significantly higher infant mortality in the districts in the dry or intermediate zones than in those entirely in the wet zone. This relationship is due to the endemicity of malaria as judged by spleen surveys; the spleen rate in the dry areas is high. Dietary surveys have shown that most of the pregnant women had an inadequate intake of proteins and consequently it is not surprising that many infants are born in a debilitated condition and that malnutrition forms an important factor in the neonatal mortality.

Malnutrition, malaria and hookworm are the 3 most important factors affecting infant mortality. The first is the most difficult to remedy since its cause is economic. The control of the other 2 factors, which has already paid dividends, will improve the nutritional status to some extent by the reduction of anaemia and will lead to improved economic conditions.

W. J. Martin

TAYLOR, W. F. **Some Monte Carlo Methods applied to an Epidemic of Acute Respiratory Disease.** *Human Biol.* 1958, Sept., v. 30, No. 3, 185–200, 1 fig. [32 refs.]

Much of the effort at the mathematical analysis of epidemics which is now nearly a century old has been in the form of deterministic models which treat infection as if it occurred in an uninterrupted space containing countless people. Recent work has remedied some of the failures of this approach by the substitution of the stochastic method in which infection is treated as occurring in limited cells or groups of people, and taking account of the laws of chance that in such conditions people might be infected or not.

[See SERFLING, *Human Biol.*, 1952, v. 24, pp. 145–166 and BAILEY, this *Bulletin*, 1956, v. 31. 106.]

The stochastic technique, though undoubtedly superior particularly when dealing with highly cellular urban populations, is difficult of application owing to its mathematical complication, the working of life-like models being virtually dependent on the availability of electronic computors. The present author, with this facility, has examined the incidence of acute respiratory disease, for which he uses a precise definition, in 117 cells or "flights" each containing 60 or 72 American airmen resident within the cell for 12 weeks, making most of their contacts within it but exposed to a certain degree of contact outside. The observed incidence of single, double, treble and further multiple admissions to hospital follows a well marked frequency curve with its maximum at the fourth week. Examination of the records shows that account must be taken of the existence of sub-clinical cases and of partial immunity conferring some degree of protection after an infection. On this basis both deterministic and

stochastic models have been created, the latter on a simplified random sampling or "Monte Carlo" basis. So far as first hospitalization is concerned, the fit achieved by both approaches is very close but neither method exactly matches the observed repeat hospitalizations. The deterministic approach gives too many particularly in the early weeks, and the stochastic in the later weeks, but even so the values of the constants deduced are of some considerable interest and the deviations from observed values lead to a useful discussion of their probable cause. [The unusually full data which were available have made it possible to produce a very clear mathematical examination which is of unusual interest.] *G. Macdonald*

BARR, R. **Hospital Admissions and Social Environment.** *Med. Officer.* 1958, Dec. 5, v. 100, No. 23, 351–4, 1 fig. [18 refs.]

This paper is based on a 2 months' survey of hospital admissions in 32 local authority areas in the 5 counties of Berkshire, Buckinghamshire, Hampshire, Oxfordshire and Wiltshire. For each speciality an age-sex standard admission ratio was found. This ratio was correlated with socio-economic indices derived from the 1951 census, the proportion in the various social classes, overcrowding, and the exclusive use of the 5 main household amenities. Most of the correlations were insignificant and the significant correlations occurred in the specialities of traumatic and orthopaedic surgery for males and females and in gynaecology. It appears that the higher social classes use the hospital services in the area more and the lower social classes less than might have been expected. *W. J. Martin*

CONGO BELGE. UNION MINIÈRE DU HAUT-KATANGA. Département Médical. Rapport Annuel, année 1957. [**Annual Report of the Medical Department, Union Minière du Haut-Katanga, 1957**] 52 mimeographed pp. & 10 pp. of folding tables. [1958.]

The European medical personnel of this large mining organization comprised 34 doctors, 48 nursing sisters of religious orders, 20 male and 31 female assistants; the African personnel included 270 nurses and students and 379 others. The working population (and families) for whom these services were provided numbered 8,623 Europeans and 123,282 Africans.

Various tables show the illnesses reported in the Europeans; perhaps the most striking feature is that in 1957 the incidence of malaria was only 1·38% against an average of 9·96% for the 10 years up to 1955 (the figure for 1946 was 48·82%).

For the Africans malaria accounted for 3·32% of all sickness in 1957 against 17·7% in 1946. Infant mortality at 57·3 per 1,000 live births compares with 123 in 1947 and with 40·7 in Belgium (1955) and 26 in England (1955). [This relatively low figure for Africans probably reflects the care taken to preserve the health of employees and their families.]

The remainder of the report consists chiefly of elaborate tables of disease incidence, which are largely of local interest. *Charles Wilcocks*

Communicable Diseases

For the bacteriology of these diseases see the section on Bacteriology below.
For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order:—General; Diphtheria, Whooping Cough, Streptococcal Infections, Staphylococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis, Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Encephalitis; Enteric Fevers.

FENNER, F. **The Seed and the Soil: Host Susceptibility in Infectious Diseases.** *Med. J. Australia.* 1958, Oct. 11, v. 2, No. 15, 477–82.

The conquest of the major infective diseases of man is in essence complete, and (if mass destruction be omitted) food and not disease becomes the ultimate limiting factor in human breeding. But non-fatal infections persist and intermittently cause ill-health, and "students of infectious disease must therefore move from the nineteenth century preoccupation with the great killing diseases and the relatively simple picture of infection leading immediately to disease (of severity varying from lethal to subclinical). They must look more thoroughly at the endemic infections of the present . . ."

In the interplay between man and the host of microorganisms to which he is exposed, the outcome will be decided by the genetic constitutions of host and invader, and the physiological state of each at the time of invasion. The writer of this Listerian Oration considers these matters in detail as they affect the host.

When it has been investigated in various strains of mice, host-resistance appears to depend on complex genetic factors, for example, in mouse typhoid and infections with 17D yellow fever and other viruses, *Plasmodium berghei* and *Mycobacterium tuberculosis*. A similar complexity underlies many of the racial or

familial reactions to disease agents in man, which are further complicated by environmental factors and the effects of acquired immunity. It may be, for example, that natural selection has virtually eliminated those susceptible to yellow fever in Africa, the ancestral home of the disease, while both man and monkey show a much wider spectrum of resistance in South America because a comparatively short time has elapsed since the virus invaded that continent. However, in rabbit myxomatosis in Australia, changes in the virulence of the organism and in the resistance of the host could both be demonstrated after only 4 host generations—a rate of adaptation that could only be induced by a highly lethal infection.

Man displays 3 clear-cut hereditary traits that influence his resistance to certain infections. Of these, acatalasaemia [a congenital deficiency of catalase in the blood] with its resultant oral ulceration remains an isolated curiosity; but the well-defined advantage of the sickle-cell trait carrier in the face of malignant tertian malaria points the way to a further exploration of the significance of the inherited anomalies of haemoglobin structure; and the remarkable susceptibility to bacteria and some viruses displayed by the subjects of aggamaglobulinaemia (which may be due to several genetic defects) offers a means of obtaining information about the role of the antibody mechanism in infectious diseases.

Many considerations show the importance of the physiological state of the host in resisting either infection or the development of overt disease. The young suffer more seriously from most infections, but less than (non-immune) adults from poliomyelitis. Many infections are more virulent during pregnancy or under cortisone therapy. Chronic malnutrition of the host, however, is not favourable to most infecting parasites, though it increases susceptibility to tuberculosis.

But so diverse are the conditions under which man may succumb to infection, or allow the activation of a latent infection, that the author sees the best hope for amelioration in what might be described as blunderbuss therapy on a global scale—that is, the steady improvement of social conditions. *Alan Raper*

PROVVIDENZA, G. L'impiego della sulfametossipiridazina in terapia **[The Use of Sulphamethoxypyridazine in Treatment]** *Acta Med. Italica.* 1958, Feb., v. 13, No. 2, 48–52. [20 refs.]

Sulphamethoxypyridazine [this *Bulletin*, 1957, v. 32, 179], a new sulphonamide, is quickly absorbed, sparingly acetylated, and slowly eliminated. Various workers are quoted on its very low toxicity to experimental animals. In man it reaches, relatively quickly, a notable concentration in the blood, which persists for a considerable time.

The author tested sulphamethoxypyridazine on 60 patients suffering from conditions sensitive to sulphonamides, at the Clinic for Infectious Diseases at the University of Rome, between November 1957 and February 1958. Of these, 22 were children under 10. There were 7 cases of bronchopneumonia, 22 of bronchitis, 8 erysipelas, 7 cases of purulent infections of the skin, 2 meningococcal meningitis, 5 tonsillitis, 2 phlebitis, 3 abscesses, 4 scarlet fever. In children the drug was administered in suppositories, 0·5 gm. being given every 12 hours for the first 2 days and then every 24 hours. In adults 2 0·5 gm. tablets were given as a first dose followed by 1 tablet every 12 hours. Treatment was continued for 4 to 14 days. Fever disappeared within 24–72 hours, and no notable side-effects or blood alterations occurred. In the meningococcal meningitis penicillin was also used for about 6 days, and for the abscesses vaccine therapy was also given. Clinical cure followed in all cases except in one patient with bronchopneumonia, aged 58, in whom fever persisted after 10 days of treatment, which was then changed to tetracycline. This patient came under notice late in the illness and had cardiac complications.

E. Agius

SUKHORUKOVA, N. L. **Factors affecting the Danger of Infection from Scarlet Fever Convalescents.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 9/10, 1468–74. [Translated from Russian.]

It appears that official permission to discharge scarlet fever patients from hospital as early as the 14th–15th day of illness has only recently been given in the Soviet Union. A number of Russian authors [no Western sources are quoted] had come to the conclusion that early discharge after scarlet fever had no adverse effect on the period of convalescence, on condition that the official hospital regime was strictly observed and penicillin treatment given early; the number of convalescents dangerous to others was not considered to be increased by this practice. [This is in good accord with British experience during the last 15–25 years.]

This article records the actual findings for 187 patients discharged from 2 Moscow hospitals for infectious diseases from October 1954 to March 1956. It was found that 11·8% of these discharged before the 16th day were dangerous to contacts at home, the corresponding figures being 12·2% for those discharged from 12th to 22nd day, 6% from 22nd to 25th day and 6·6% after the 30th day. The authors concluded that early discharge (14th to 21st day of disease) was reasonable only when all the conditions laid down in the regulations were strictly observed. [This article has little relevance to conditions in Britain, although the clinical type of the disease itself may be roughly comparable—75·5% mild, 24·5% moderate, none severe. Penicillin was given only to 61·5% for the patients in hospital, thus permitting a large proportion of the patients at the time of discharge (over 60%) to remain or become carriers of haemolytic streptococci, many being cross-infected with different types from that present on admission. Add to this unsatisfactory state on discharge, the absence of adequate clinical examination for freedom from complications, and the fact that 75% of the families to which the patients were discharged occupied only 1 room—and the reason for the poor results becomes apparent. Again the bed space per patient in the hospitals was only 2 to 4 square metres, compared with the official standard of 16 square yards

in Britain rarely reduced in practice below 10 square yards in British hospitals for infectious diseases.]

H. Stanley Banks

KODAMA, T., MIYAMOTO, Y., KOTAKE, I. & OCHIAI, S. **Epidemic Nephritis in Japan.** *Yokohama Med. Bull.* 1958, June, v. 9, No. 3, 105–18, 4 figs. [91 refs.]

After a few minor epidemics in various areas of Japan in recent years, an explosive epidemic of acute nephritis involving the whole of Japan occurred in the autumn of 1955, and recurred in various districts in the autumn of 1956; these were associated particularly with group A streptococcal infection of types 4, 12 and 6. It is likely that some at least of these nephritogenic types were imported some 2 or 3 years previously. Almost all the Japanese patients were children, mainly between 5 and 10 years old. Males slightly outnumbered females. In some districts the attack-rate in schools was exceedingly high—30–40% in some instances. The household attack rate was of the order of 15 %—similar to that of scarlet fever. The fatality rate was 0·95%—about 3 times that of scarlet fever. The time required for recovery was about 1 month on average. Prognosis was generally favourable, but some patients developed chronic nephritis.

The bacterial factor involved in this epidemic was mainly the prevalence of streptococcal epidemics of types 4, 12 and 6; the main host factors concerned were presumed to be an exceedingly low mass immunity to these streptococcal types among children, as well as high concentration of non-immunes, especially in children's institutions. Good results were obtained in the prevention of spread of the acute nephritis in at least one children's institution, by the timely injection of 600,000 units of benzathine penicillin into all inmates at the commencement of an outbreak.

H. Stanley Banks

GILLESPIE, W. A., SIMPSON, K. & TOZER, Rosemary C. **Staphylococcal Infection in a Maternity Hospital. Epidemiology and Control.** *Lancet.* 1958, Nov. 22, 1075–80, 2 figs. [26 refs.]

This paper reports a 2½ years' investigation of staphylococcal infection in the Bristol Maternity Hospital. As has been found elsewhere over half the infants had become umbilical or nose carriers of *Staphylococcus aureus* by the 2nd day of life, the umbilicus commonly being infected before the nose. The carrier rate for both sites reached 90% before discharge at the 10th day, but there was some tendency for the umbilicus to lose its staphylococci during the 6th–10th days. 69% of the staphylococci from infants were penicillin-resistant but only about 13% were resistant to other antibiotics as well. A temporary increase in the use of streptomycin for a short period was followed by an increase in the number of streptomycin-resistant strains. Most of the infants' staphylococci fell into phage groups I and III, the former being slightly the commoner in the nose, and the latter on the umbilicus. Types 52A/79, 80 and 71 were the commonest types associated with skin sepsis.

In a 10-month period 11·8% of 842 infants developed staphylococcal lesions while in hospital. 20% of infants who were nose and umbilical carriers on the 2nd day of life developed sepsis, compared with only 1·4% of those who were non-carriers. With colonization of the umbilicus alone, the rate was 3·2%.

Disinfection of the infants' bedding with Cirrasol [this *Bulletin*, 1955, v. 30, 897] had no effect on the rate of acquisition of staphylococci, or of sepsis.

The use of a chlorhexidine (Hibitane) [*ibid.*, 1958, v. 33, 390] hand cream by the nurses each time they washed reduced the rate of acquisition of staphylococci by the babies, and may have reduced the incidence of sepsis.

Finally a trial was made of a hexachlorophane [*ibid.*, 1957, v. 32, 1129] dusting powder, applied to the umbilicus whenever the napkin was changed. This led to a pronounced fall in the rate at which the nose and umbilicus acquired staphylococci and there was a strong suggestion that the sepsis rate was also reduced.

R. E. O. Williams

TIMBURY, Morag C., WILSON, T. S., HUTCHISON, J. G. P. & GOVAN, A. D. T. **A Staphylococcus Type-80 Epidemic in a Maternity Hospital illustrating some Special Features.** *Lancet.* 1958, Nov. 22, 1081–4. [11 refs.]

In a maternity hospital in which a bacteriological survey was already in progress, a sudden increase in the incidence of serious staphylococcal infection occurred among the babies. This was shown to be associated with the introduction of a type 80 staphylococcus into the hospital, and 14 of the 18 infections occurring during the epidemic were due to this strain, as were all the 9 serious infections. There were 8 deaths, almost all with pneumonia; 6 were associated with type 80.

About 6 weeks after the first case, the hospital was closed and 475 members of the staff were swabbed. Only 3 were carriers of type 80; 2 of the carriers were nurses who also had boils, but were probably victims rather than sources of the epidemic spread. There was, surprisingly, practically no contamination of the environment with the epidemic type.

21 of the 99 babies born in the last 2 weeks of the hospital epidemic developed lesions after discharge but only 4 of the 16 cultures obtained proved to be type 80, although 10 of them were penicillin-resistant and so probably acquired in hospital. 4 months after discharge, 2 of 16 babies who had been colonized by type 80 while in hospital were still nasal carriers [throat swabs were apparently not done].

R. E. O. Williams

GOSLINGS, W. R. O. & BÜCHLI, K., with the technical assistance of H. I. SCHUDDEBOOM. **Nasal Carrier Rate of Antibiotic-Resistant Staphylococci. Influence of Hospitalization on Carrier Rate in Patients, and their Household Contacts.** *Arch. Intern. Med.* 1958, Nov., v. 102, No. 5, 691–715, 2 graphs. [47 refs.]

57% of 587 patients carried coagulase positive staphylococci in their noses on discharge from the

surgical department of University hospital of Leyden. 66·5% were penicillin resistant and belonged predominantly to phage group III, the penicillin sensitive strains were equally divided between groups I, II and III. The carrier rate of resistant strains rose with the length of stay in hospital.

Antibiotic treatment of an individual favoured the colonization of his nose with a strain resistant to that antibiotic and the change to the resistant hospital staphylococcus took place especially in the first 2 weeks in hospital. Patients leaving hospital with a sensitive strain had received antibiotic therapy less often than those leaving with a resistant strain. There was some evidence that some people are constant nasal carriers and some constant non-carriers.

After discharge from hospital the resistant hospital strain was lost quickly, and in the majority of cases this was not replaced by another strain. In the group of patients discharged with resistant strains, the sensitivity to penicillin of strains subsequently isolated fell to that of the normal population in 6–12 months. The sensitivity to chloramphenicol fell to normal in 3 months partly owing to loss of resistant strain but partly owing to back-mutation to sensitivity. The resistance to tetracycline and streptomycin of strains isolated from this group was higher than normal 1 year after discharge.

Patients having a sensitive strain on discharge lost the strain more slowly than those carrying a resistant one—these may have been persistent carriers of one type. Only rarely did patients who were discharged free from pathogenic staphylococci subsequently acquire them.

Transfer of resistant strains by discharged carriers to home contacts occurred only in 11% of families and 8% of household contacts, but contact in some way with hospital environment accounted for 60% of resistant staphylococci found in family contacts.

[The authors state that their bacteriophage NO adapted from bacteriophage 42E was similar to bacteriophage 80 adapted from 42E, by ROUNTREE and FREEMAN, this *Bulletin*, 1956, v. 31, 334. Bacteriophage 80 was adapted from bacteriophage 52A and is serologically different from 42E. Bacteriophage 81, whose lytic spectrum resembles that of bacteriophage 80 was adapted by COMTOIS from bacteriophage 42B.]

M. Patricia Jevons

KÖHLER, W. Der Antistreptolysin-Normaltiter in NO-Deutschland. Untersuchungen an 600 Personen. **[The Anti-Streptolysin Titre of Normal Persons in North-East Germany. Examinations of 600 Persons]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, July–Aug., v. 116, Nos. 1/2, 145–52, 2 figs. [11 refs.]

Sera from 600 patients suffering from non-streptococcal disease were examined for antistreptolysin titre by KALBAK's method. Of the 489 up to 60 years of age, 18·7% had a titre of 200 units or more, and 8·2% a titre of more than 250 units per ml. Older people had rather lower titres. Season had no effect. From this and other work it is suggested that the normal titres should be taken as 150 units from 5 months to 5 years, 250 from 6 to 59 years, and 200 for 60 and over.

R. E. O. Williams

JOHANOVSKÝ, J. Die Bedeutung des Antileukozidins und Antitoxins bei der Immunität gegen Staphylokokken-Infektionen. **[Significance of Antileucocidin and Antitoxin in Immunity against Staphylococcal Infections]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, Oct., v. 116, No. 4, 318–28. [29 refs.]

Estimations were made of the staphylococcus antitoxin and antileucocidin titre of the serum of normal women and their newborn infants, and the results analysed in relation to the experience of staphylococcal infections in mother in the first 3 months and her infant in the first 2 months after birth.

There was no clear association between the antitoxin and antileucocidin titres; about 17% of mothers had antitoxin titres of 2 units per ml. or more [which is more than usually found]. Sepsis in the infants was not related to their antitoxin titre, but was less common in the infants with the higher antileucocidin titres. Mastitis and fever (thought generally to be due to staphylococcal vaginal infection) was also less common in the mothers with the higher antileucocidin titres.

Immunization of the mothers during pregnancy with an anatoxin adsorbed on aluminium hydroxide increased the antitoxin and antileucocidin titres of both mother and infant; an antileucocidin titre of 2 units per ml. or more appeared substantially to protect against infection.

R. E. O. Williams

DE FRANCO, V. J. **The Efficacy of Erythromycin in the Control and Prevention of an Endemic Staphylococcal Infection in a Large Private Hospital Nursery.** *Antibiotic Med.* New York. 1958, Sept., v. 5, No. 9, 573–7. [10 refs.]

In the late spring of 1956 an epidemic of infection due to a staphylococcus of phage type 42B affecting both mothers and infants, developed at the Good Samaritan Hospital, Cincinnati, Ohio, and several infants died of pneumonia. All infants were then given erythromycin for 7 days after birth (50 mgm. 2 or 3 times a day according to weight) and all carriers among the staff were given 1 gm. daily for 7–10 days. Of "300 cultures of personnel" 18 from staff in the nursery, 1 in the delivery room and 10 paediatric staff were positive. This régime was continued for 35 days, during which 648 infants were treated. No further staphylococcal infection occurred. No acquisition of resistance was observed, "since all follow-up cultures were negative". This method of arresting an epidemic is commended as removing the necessity for closing a maternity unit on account of sepsis. [The author does not say for how long this unit remained free of infection. The number of carriers found is surprisingly small, but it is not clear whether the figures given refer only to the epidemic type of staphylococcus or to pathogenic staphylococci in general.]

L. P. Garrod

KASPAROVA, T. I. **Epidemiology of Measles and Whooping Cough.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 7/8, 1188–93, 3 figs. [10 refs.] [Translated from Russian.]

To those who hope to find some new ideas, or at least a new orientation of ideas, in articles translated from the Russian this one is disappointing. It is on an elementary level, contains nothing new, and omits much that might have been discussed. An investigation is described into the spread of measles and of whooping cough in an over-crowded residential institution for children, where the beds were so close as to be " practically touching each other ". In these circumstances when the infections were introduced one after the other, nearly all the susceptible children contracted the diseases, rapidly and *en masse* in the case of measles, and more slowly and gradually in the case of whooping cough. This difference is attributed to the relatively low dispersion of infected aerosol around the child with whooping cough owing to the high viscosity of the coughed-up bronchial secretions, as compared with that of the sneezed-out and coughed-up nasopharyngeal secretions in measles. The earlier involvement of children in the epidemic process in whooping cough, as compared with measles, is attributed to the mobility of children with whooping cough, its late diagnosis, and to its abortive forms. [Nothing is said about whooping cough in the first few months of life, occurring probably in spite of some passive humoral immunity from the mother, or of the related fact that whooping cough is more a local and less a general disease than measles.] *H. Stanley Banks*

JACKSON, A. D. M. & FISCH, L. **Deafness following Maternal Rubella. Results of a Prospective Investigation.** *Lancet.* 1958, Dec. 13, 1241–4, 2 figs. [11 refs.]

A national prospective inquiry carried out by the Ministry of Health into the effects of virus infections during pregnancy [not yet published] included 79 surviving children from the counties of London and Middlesex whose mothers had rubella during the first 18 weeks of pregnancy. 57 of these children were still available and were given detailed hearing tests with audiograms when between the ages of 3 and 5 years, together with 57 matched controls. 15 of the former group had major congenital defects which included 12 with congenital deafness alone, 2 with congenital deafness combined with other defects and 1 with defects of the eye only. No defects were observed in children whose mothers had rubella in the 17th and 18th weeks of pregnancy but of the 46 in whom rubella had occurred during the first 16 weeks of pregnancy 14 (30·4%) had congenital deafness (6 bilateral and both ears severe, 3 bilateral and 1 ear slight, and 5 unilateral and severe). No case was found in the control group. 9 of the 14 cases had not been detected at previous clinical examinations at the age of 1 and 2 years. Examinations at an earlier age than 4 years and without hearing tests therefore seriously understate the incidence of deafness after rubella.

[See also this *Bulletin*, 1958, v. 33, 551.]

A. Bradford Hill

SCHREUS, H. T. Erythema infectiosum (Megalerythema epidemicum). Epidemie in Westdeutschland. **[An Epidemic of Infectious Erythema (Epidemic Megalerythema) in Western Germany]** *Deut. med. Woch.* 1958, Dec. 5, v. 83, No. 49, 2165–7, 3 figs.

In this paper the author discusses some of the features of erythema infectiosum which recently produced a mass epidemic in Western Germany. In the absence of compulsory notification of the disease the real magnitude of the epidemic could not be determined but it appears to have been much greater even than the one in Breslau in 1913–14 when over 1,000 cases were estimated to have occurred. Erythema infectiosum (known also as megalerythema epidemicum, *ringelröteln, grossfleckenkrankheit* or simply fifth disease) is not familiar to all practising doctors but its diagnosis should not cause much difficulty. A description of the typical characters of the disease is given with several photographs of cases with an extensive rash. The aetiology of the disease is as yet uncertain although the isolation of a causative virus has been claimed. Treatment of patients and the measures to be taken in times of epidemic are shortly considered. No evidence has as yet been presented of any damage to the foetus resulting from the infection in pregnant women. The present epidemic differed from others in the past in its high incidence over a wide area, in that adults were most frequently attacked and more women than men or children were infected. Other differences were the frequency of itching, occasionally high fever and oedema, vesicles on the extremities which were sometimes confluent, exanthemata on the palms of the hands and soles of the feet, leucocytosis of 7,000 to 22,000 and eosinophilia of between 5 and 10%. *M. E. Delafield*

HORTON, G. E. **Mumps Myocarditis: Case Report with Review of the Literature.** *Ann. Intern. Med.* 1958, Nov., v. 49, No. 5, 1228–39, 6 figs. [24 refs.]

ZILIȘTEANU, C., ILIAN, I., MĂNESCU, C. & IONESCU, Honorina. Considerații asupra unei epidemii de tuse convulsivă în mediul rural. **[A Whooping-cough Epidemic in a Rural Area]** *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, Mar.–Apr., v. 3, No. 2, 171–8, 7 figs. English summary (5 lines).

An account is given of an epidemic of pertussis which occurred in a rural area in Rumania in the summer of 1949, with a total of 268 cases. The incidence based on a population of 651 children aged up to 15 years was 43·68%; 73 cases (27·24%) were mild, 130 (48·54%) moderate and 14 (5·22%) severe. Respiratory complications occurred in 91 (33·9%) and neurological

complications in 36 (13·4%) cases; the mortality was 1·22% (8 cases) based on the child population, with a case mortality of 2·98%. An attempt was made to treat the disease by vaccination during the catarrhal stage.

D. J. Bauer

IVAN, I. M. & ABABEI, R. Date epidemiologice privind evoluţia tusei convulsive in Bucuresti între anii 1952 si 1956. [**Epidemiological Data concerning the Evolution of Whooping-Cough in Bucharest between 1952 and 1956**] *Microbiol., Parazitol. si Epidemiol.* Bucharest. 1958, Mar.–Apr., v. 3, No. 2, 179–85, 4 figs. English summary.

The incidence of pertussis in Bucharest has risen considerably since 1952 with increases in incidence over the preceding year of 6·2%, 54% and 73·4% in 1953, 1954 and 1955 respectively. In 1956 the incidence fell by 25%. The increase is attributed partly to better notification of cases, but mainly to the absence of effective prophylaxis, and during the period under review the disease has taken on an epidemic character. The maximum incidence was observed between June and August, with a peak lying between that of measles (June) and scarlet fever (October–November), and the total duration of each epidemic wave was about 15 months. Most cases (61·4–66·2%) occurred in children aged up to 3 years; the mortality ranged from 0·67 to 1·3 per 1,000.

D. J. Bauer

BERG, J. M. **Neurological Complications of *pertussis* Immunization.** *Brit. Med. J.* 1958, July, 5, 24–7. [37 refs.]

A child 8 months old, within 24 hours of a combined diphtheria-pertussis inoculation, became pyrexial, drowsy and hypotonic, and subsequently had convulsions accompanied by mental deterioration. The author reviewed the literature for similar neurological complications of pertussis inoculation. There were 107 cases, mostly in males, and reactions occurred in all age groups irrespective of dosage and type of vaccine used. Follow-up of the cases revealed a recovery rate of 50%, a persisting morbidity (physical or mental) rate of about 30% and a mortality rate of about 15%.

The question of aetiology is considered and contra-indications are discussed. The value of pertussis immunization is emphasized, as is the grave danger of further inoculations when a previous one has produced any suggestion of a neurological reaction.

F. T. Perkins

MARTIN DU PAN, R. **The Vaccination of the Newborn Infant against Pertussis.** *J. Pediatrics. St. Louis.* 1958, Aug., v. 53, No. 2, 180–86, 5 figs. [27 refs.]

Since PITTMAN (*J. Wash. Acad. Sci.*, 1956, v. 466, 234), has pointed out that the greatest proportion of deaths due to whooping cough in the United States in the years 1936–45 occurred in infants under 5 months of age, the author studied the possibility of immunization in the newborn infant. 3 groups of infants were studied; those in group 1 were 1–15 days old, those in group 2 were 1 month old, and those in group 3 were between 6 and 26 months old at the time of having their first dose of pertussis vaccine. The serological response greatly increased with increase of age and with the infants in group 1 the response was unsatisfactory. This lack of response, especially during the first month of life, was correlated with the inability of a newborn infant to produce beta globulins and as a result of these studies it is suggested that pertussis vaccination should not start until after the fourth week of life.

F. T. Perkins

THOMPSON, C. A. & CANTRELL, F. P. **Chickenpox Pneumonia treated with Prednisolone: a Case Report.** *Ann. Intern. Med.* 1958, Nov., v. 49, No. 5, 1239–46, 4 figs. [27 refs.]

The role of steroids in the treatment of virus diseases is still uncertain. In the case here reported prednisolone therapy was instituted only after general supportive measures and antibiotics appeared to be failing and the patient was desperately ill. Recovery was seen to commence within 24 hours and the dose of prednisolone, initially 40 mgm. daily, was gradually reduced over the ensuing 2 weeks. Serial X-ray films show widespread nodular infiltration throughout both lung fields which had almost completely cleared 3 weeks later.

J. Pickford Marsden

PROC. ROY. SOC. MED. 1958, Dec., v. 51, No. 12, 1009–18 (Sect. Epidem. & Preventive Med. 29–38), 4 figs. [23 refs.] **Symposium on the Asian Influenza Epidemic, 1957** [PAYNE, A. M. M.; MCDONALD, J. C.].

Historical and epidemiological aspects of the 1957 influenza pandemic are authoritatively reviewed by A. M.-M. PAYNE (*Some Aspects of the Epidemiology of the 1957 Influenza Pandemic*). Data on the origin and the main routes of spread of the pandemic are presented and illustrated in a world map. The influence of different means of travel on the rate of spread of the pandemic is discussed in comparison with previous pandemics. The effect of crowding on the initiation of local epidemics is pointed out and the morbidity and mortality rates observed in different populations and age-groups are presented. Fatal cases of Asian influenza were usually associated with secondary bacterial infections caused in a great proportion of cases by staphylococci. Some deaths, especially in the younger age-groups, were apparently due to the primary virus infection but were not associated with virus strains with increased pneumotropism. The possible relation of the Asian influenza virus with the agent responsible for the 1889–90 pandemic [MULDER & MASUREL, this *Bulletin*, 1958, v. 33, 635] is discussed in detail and alternative explanations for the findings on which this hypothesis is based are presented.

It is finally pointed out that during the first 4 months of 1958 a relatively low incidence of Asian influenza has been accompanied in several countries by high

mortality attributed to influenza and pneumonia. Strong evidence suggesting that this high mortality results from infections by Asian influenza virus is presented by J. C. McDonald (*Asian Influenza in Great Britain 1957–58*). This evidence is based on laboratory reports of positive tests for influenza, on mortality and sickness claims statistics and on the results of special epidemiological and serological surveys. The results suggest that the higher mortality observed in early 1958 was due to increased prevalence of infection in older age-groups. *H. G. Pereira*

Fraser, P. K., Hatch, L. A. & Hughes, K. E. A. **The Pattern of the Influenza Outbreak in the Portsmouth Naval Command, 1957–8.** *J. Roy. Nav. Med. Serv.* 1958, v. 44, No. 4, 285–91, 1 graph.

An outbreak of Asian influenza occurring in the Royal Navy, Portsmouth Command, was investigated by clinical and laboratory methods. The outbreak covered the period from August 1957 to January 1958, with a peak between mid-September and late-October, during which an attack rate of 1 in 4 was observed and approximately 6,000 cases were reported. Acute and convalescent sera from 615 patients were tested by complement-fixation and showed significant antibody rises against influenza A in 386 pairs, influenza C in 9 pairs, influenza A and C in 1 pair and adenovirus in 4 pairs. 4-fold or greater rises in haemagglutination-inhibition titres against Asian influenza strains were detected in 47 of 53 serum pairs with rises in complement-fixing titres for influenza A. 13 virus strains isolated from throat swabs were found to belong to the Asian group of influenza virus.

The main symptoms observed during the outbreak were typical of influenza, consisting of pyrexia, headache, cough and general myalgia, except in one centre where the clinical picture changed during November and most patients showed gross tonsillar inflammation and rhinorrhoea. *H. G. Pereira*

Hers, J. F. P., Masurel, N. & Mulder, J., with the technical assistance of E. Degger, L. v. d. Kuip, M. Meuleman, A. Peters, W. Tom, F. Heemskerk & P. Webbers. **Bacteriology and Histopathology of the Respiratory Tract and Lungs in Fatal Asian Influenza.** *Lancet.* 1958, Nov. 29, 1141–3, 1 fig. [16 refs.]

A strain of Asian influenza virus was isolated from lung tissue in 106 fatal cases of Asian influenza and from the trachea in 15. Ferrets inoculated intranasally with lung tissue from 20 cases developed a positive haemagglutination inhibiting titre to the Asian virus. In all, in 70% of the autopsies which were considered to be cases of fatal influenza, influenza virus could be shown to exist. The histopathological picture in many cases was very suggestive of pure influenza virus pneumonia and resembled that of 1918 influenzal pneumonia.

The 1918 pandemic was caused most probably by the swine A type virus and the high mortality during the second wave was presumably due to development within a few months of high pneumotropic virulence. It is possible that the virus of the 1957 pandemic as well as that of the 1918 pandemic originated from an animal carrier (swine ?) in which the strain developed non-sensitivity to beta-inhibition associated with a potential pneumotropic affinity. Neither the 1889 nor the 1957 pandemic, which may be virologically related (pointing towards a possible animal reservoir in Asia), was rapidly followed by a severe pneumotropic wave. A possible second wave of Asian influenza may be expected in the near future which will perhaps shed light on this difference from 1918 influenza. Although the Asian influenza virus has shown a potential pneumotropism for human lung tissue the pneumotropic virulence so far is low.

The most common secondary invader of the lungs was a coagulase positive *Staphylococcus aureus* which was isolated from about 60% of the cases.

P. A. Clearkin

Gundelfinger, B. F., Stille, W. T. & Bell, J. A. **Effectiveness of Influenza Vaccines during an Epidemic of Asian Influenza.** *New England J. of Med.* 1958, Nov. 20, v. 259, No. 21, 1005–9, 2 figs.

Protection against epidemic Asian influenza by killed influenza virus vaccines was tested in 3,355 recruits forming part of the population of a naval training centre. The recruits under study were randomly divided into 3 groups consisting of approximately 30%, 30% and 40% of the study population each receiving a monovalent Asian influenza vaccine containing 200 chick-cell agglutinating (CCA) units (vaccine A), a polyvalent vaccine containing 250 CCA units each of A/Swine, A-prime (FM1) and B (Great Lakes) influenza viruses (vaccine B) and a placebo. A sharp outbreak of Asian influenza was observed shortly after the period of vaccination. The protection conferred by vaccination was evaluated on the basis of the number of recruits reporting to the infirmaries with febrile respiratory illness 2 weeks or more after inoculation. Attack rates were 23·5, 49·7 and 58·9 per 1,000 per week for the groups receiving vaccine A, vaccine B and placebo respectively. Effectiveness of vaccination was estimated as 60% for vaccine A and 16% for vaccine B. When only the 2 weeks of highest total incidence of respiratory illness were analysed, effectiveness of vaccines A and B was estimated as 83% and 21% respectively. The protective effect of vaccine A was already marked 10 days after vaccination.

It is concluded that both vaccines conferred some protection but the use of a vaccine containing a virus strain homologous to the current epidemic strain is essential for maximum prophylactic effectiveness.

H. G. Pereira

Sulman, F. G. **Chloramphenicol and Control of the Common Cold.** [Correspondence.] *Lancet.* 1958, Dec. 20, 1335–6.

This is a controversial letter. First, the author proposes antibiotic treatment of the common cold and

sore throat over a period of 3–5 days, on the grounds that there is a risk of secondary disease, especially acute nephritis, as well as loss of working time when the patient is incapacitated. Secondly, he recommends chloramphenicol on account of its superior antibiotic activity, its low tendency to induce drug-resistant strains, the absence of allergic reactions, and, contrary to the general impression, its safety. He challenges, on statistical grounds, the prevalent belief that chloramphenicol may be a cause of aplastic anaemia, referring to E. A. Brown (*Ann. Allergy*, 1956, v. 14, 206), quoting Haviland, who calculated that the incidence of aplastic anaemia in the general population exceeds that reported from chloramphenicol administration. Experience in Israel, he states, fully justifies this opinion, and he stoutly maintains that there is no justification for restricting the use of this effective drug.

In the last 4 years 2 trials were made in Jerusalem. In the first, 60 patients were given a total of 3·5 gm. chloramphenicol in diminishing amounts spread over 5 days, and 56 were able to carry on routine work, while the symptoms progressed in 38 of 40 control patients given a placebo. In the second trial, 20 patients were given 10–14 lozenges containing 30 mgm. chloramphenicol palmitate daily for 2–3 days. As this preparation proved to be inactive *in vitro*, it was assumed that the result—suppression of the symptoms in 16—was not due to a local effect, but to the absorbed drug; on this assumption it was considered that chloramphenicol in doses of 150–200 mgm. daily may suppress the infection. [In such a controversial matter the evidence, as presented in this letter, is much too slender to be convincing.] *H. Stanley Banks*

Wheeler, J. E., Plotkin, R. F., Fromme, Dalores & Smith, Nancy. **Acute Upper Respiratory Disease: Clinical and Bacteriological Response to Short-Term Treatment with Penicillin V.** *J. Pediatrics.* St. Louis. 1958, Nov., v. 53, No. 5, 571–8, 1 fig. [12 refs.]

An attempt was made, by clinical observation and quantitative bacterial methods, to evaluate oral penicillin V therapy in the common upper respiratory infections seen in children in Philadelphia between early April and mid-September; the most frequent clinical types were tonsillitis, pharyngitis, otitis media and cervical adenitis, and all the patients were ill, though not severely ill. All the common nasopharyngeal organisms were represented in the material. Treatment was by 250 mgm. penicillin V every 8 hours over 4 or 5 days for patients over 30 lb. in weight. There were no serious reactions and only 2 maculopapular rashes.

Of the 76 children treated there were excellent responses in 75. Smears and cultures of pharyngeal exudate showed a significant decrease in Gram-positive organisms after 24 hours' treatment. The method is thought to be safe and effective and useful in preserving rapport between doctor and child-patient. [The common cold does not seem to be included in this investigation.] *H. Stanley Banks*

Navrátilová, A. Naše zkušenosti s konservativní léčbou plicních hlíz endobronchiální aplikací antibiotik. **[Our Experience with the Conservative Treatment of Lung Abscesses by Endobronchial Administration of Antibiotics]** *Časopis Lékařů Českých.* Prague. 1958, Aug. 29, v. 97, No. 35, 1106–13. [13 refs.] English summary.

In the Czechoslovak Hospital in North Korea cases of lung abscess are frequently seen, which arise as a result of inadequate domiciliary or out-patient treatment of croupous pneumonia, and in view of the lack of facilities for thoracic surgery in Korea the author has developed a conservative method of treatment. After the parenteral administration of antibiotics for a few days and determination of bacterial sensitivity antibiotic solutions were instilled directly into the abscess cavities by bronchoscopy. The treatment was carried out 2 or 3 times weekly and was well tolerated; 32 patients were treated in all. The best results were obtained with acute abscesses, which healed after 6–8 weeks (14 patients). In 12 patients with subacute abscesses treatment for 2–3 months was required; 4 were completely cured and 7 had residual sputum of moderate or slight amount and fibrosis. Patients with chronic abscesses were treated for 3–6 months; 1 was completely cured, 3 were discharged improved and 1 died with gangrene of the lung. The clinical data of all the patients are given in 4 pages of tables.

D. J. Bauer

Schafer, I. A. & Mosley, J. W. **A Study of Viral Hepatitis in a Penal Institution.** *Ann. Intern. Med.* 1958, Nov., v. 49, No. 5, 1162–77, 1 fig. [15 refs.]

A detailed study on the incidence of viral hepatitis in a prison in the United States was carried out in an 11-month period from August, 1955 to June, 1956. There is a description of the prison which had in the period 1950 to 1955 an inmate population of 1,845 to 2,474. Turnover of the population is rapid. The yearly number of probable cases of viral hepatitis in the period 1945–53 ranged from 0 to 5 but in 1954 there were 17 cases and in the first 7 months of 1955 there had been 17. In the course of the study 50 patients suspected of having viral hepatitis were admitted to the prison hospital. A table sets out the frequency of clinical signs and symptoms exhibited by the 45 out of the 50 men who were definitely diagnosed as having viral hepatitis on the criteria of diagnosis which were adopted. Diagnosis was accepted as definite if 3 of the following criteria were fulfilled: (1) a compatible history, (2) icterus, (3) other signs on physical examination indicative of acute liver disease and (4) compatible laboratory data. Sections of the report deal with clinical characteristics and some case reports, population data, and epidemiological data on morbidity rate (estimated for the 11-month period as 18·9 per 1,000), distribution by race, age and dormitory.

The possible transmission of the infection is considered at length with the conclusion " that parenteral transmission of the serum hepatitis virus via contaminated syringes and needles caused the outbreak ". A table sets out the frequency of exposure to possible

parenteral transmission and the most important of these risks lies in the illicit use of drugs. Information from inmates indicated that amphetamine tablets and barbiturate capsules were sold illicitly within the prison and the drugs, after crushing in tap water, were administered intravenously by the owner of a syringe and needle for a fee as reimbursement for the risk assumed. Between injections the syringe and needle were occasionally rinsed in boiling water. In the 45 patients there were 35 who appeared to have run this particular risk of infection. *M. E. Delafield*

LIPPI, M. & SEBASTIANI, A. Variazioni dei livelli transaminemici nel corso dell'epatite virale umana. [**Changes in Serum Transaminase Contents in Human Viral Hepatitis**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1958, July, v. 39, No. 7, 431–45, 5 figs. [21 refs.] English summary (9 lines).

Many animal tissues contain glutamic-oxalacetic transaminase, also known as aspartic-ketoglutaric transaminase, and glutamic-pyruvic transaminase, also called alanine-ketoglutaric transaminase. These are present in all cells, regulating the reciprocal concentration of amino-acids and keto-acids.

It has been established [see, for example, this *Bulletin*, 1956, v. 31, 889] that human viral hepatitis is characterized by a marked increase of aspartic-ketoglutaric and alanine-ketoglutaric transaminases and by an inversion of the normal ratio between the first and the second which in healthy subjects never falls below unity, and that these findings can have clinical significance. These changes do not occur in other liver dysfunctions, except in carbon tetrachloride poisoning; moreover, unlike other changes, they appear early and persist for long.

The authors studied these changes in 36 patients between the ages of 17 and 55, of whom 25 were in the acute stage and 11 in the phase of resolution, using the method of Reitman and Frankel. In the first there was an average content of 468 units of glutamic-oxalacetic transaminase and of 690 of glutamic-pyruvic transaminase, giving a ratio of 0·68. In the second group there was an average content of 112 units of glutamic-oxalacetic transaminase and of 175 units of glutamic-pyruvic transaminase, giving a ratio of 0·69. Between 50 and 60 days after the onset of the illness the transaminase contents tended to return to normal.

The authors favour the hypothesis that the passage of transaminases into the circulation is a mechanical result of the diffuse liver necrosis, while the different extent to which both enzymes are affected must be due to some other factor affecting their release from the blood. *E. Agius*

LIPPI, M. & SEBASTIANI, A. Tassi transaminemici e prove di funzionalità epatica nella diagnostica della epatite virale e di altre epatopatie acute. [**Transaminase Serum Levels and Liver Function Tests in the Diagnosis of Virus Hepatitis and Other Acute Liver Diseases**] *Arch. Ital. Sci. med. Trop. e Parassit.* 1958, July, v. 39, No. 7, 470–80, 3 charts. [29 refs.]

This paper deals almost wholly with work already reported upon in the previous paper. 3 more cases of virus hepatitis are referred to and there are reports upon other pathological conditions of the liver in 20 cases (cholangitis, jaundice due to allergy, to enterohepatotoxic causes and to infectious mononucleosis). The conclusion is reached that the changes described in the transaminases are useful diagnostically, running parallel with the results of other liver function tests (blood bilirubin level, the Hanger and McLagan reactions, and C-reactive protein estimations). *E. Agius*

BOWERS, H. J., Jr. & ELSTON, J. T. **Listeria Meningitis. Report of a Case.** *Amer. J. Clin. Path.* 1958, Nov., v. 30, No. 5, 447–51. [23 refs.]

ANDRÉ, L.-J. & ANDRÉ-GADRAS, E. 16 cas de poliomyélite observés dans un district de brousse du Gabon. [**16 Cases of Poliomyelitis in a Bush Village of Gabon**] *Méd. Trop.* Marseilles. 1958, July–Aug., v. 18, No. 4, 638–41.

This is an account of an outbreak of poliomyelitis from July to November 1957 in an African village: 13 of 16 patients were under 5 years old. 8 of the patients had severe respiratory symptoms and 7 of these patients died: in 6 there were well-marked signs of encephalitis including coma and diffuse signs of encephalitis were found in the brains at autopsy. Poliovirus was isolated from the faeces in 2 cases. Steps taken to prevent spread included the isolation of the village, and surveillance of water supplies against faecal contamination, and vaccination, village by village, against poliomyelitis. *A. B. Christie*

SEAL, S. C. **A Note on the Outbreak of Poliomyelitis in the Andamans in 1957.** *Indian J. Pub. Health.* 1957, July, v. 1, No. 3, 187–94, 2 maps & 1 graph.

An outbreak of poliomyelitis in Port Blair, Andaman Islands, started at the end of December, 1956, and ended in May, 1957. There were 33 cases and the peak incidence was in March. Sporadic cases of poliomyelitis had occurred previously in the Andaman Islands, and in this outbreak no patient was over 8 years old. There were no multiple cases in households and apart from a group of 7 children who had all attended the children's hospital within 10–15 days of onset there was no connexion between cases. It was thought that the virus spread by faecal contamination. During the early months of 1957 the rainfall was very low, and drought conditions prevailed. The drains are open and depend on the rains for adequate flushing, and the drought resulted in filthy conditions. 29 sera of persons over 11 were found with 1 exception to contain neutralizing antibody to all 3 types of poliovirus. *A. J. Beale*

HATCH, L. A., HUGHES, K. E. A. & PILFOLD, J. N. **Observations on the Excretion of Type 1 Poliovirus from Cases and their Contacts.** *Amer. J. Med. Sci.* 1958, Oct., v. 236, No. 4, 419–24, 4 figs.

The duration of excretion of poliovirus in the faeces was studied by examining weekly samples of faeces

from 93 cases of poliomyelitis and 97 healthy contacts from whom Type 1 poliovirus had been recovered. 69 of the patients and 80 of the contacts were followed until a negative stool sample was examined. It was found that the rate of clearance of poliovirus from both groups was exponential, the logarithm of the percentage of excretions falling in a straight line against time. The percentage of excreters declined to 50% in 3 weeks for patients and 5 weeks for contacts (after onset of disease in index case); 10% of the patients were still excreting virus at 8 weeks and of the contacts at 10 weeks. Since HeLa cells were used for the examinations it is considered that the duration of excretion was probably underestimated. These findings show that a period of 3 weeks' quarantine is too short. However it is as yet uncertain that the danger of acquiring infection from a faecal excreter remains constant throughout the period of excretion. The authors do not recommend an extension of the quarantine period in view of their findings. *A. J. Beale*

BROWN, G. C. & CARROLL, Catherine J. **Antibody Response of Pregnant Women to Poliomyelitis Vaccine and Passive Transfer to Infants.** *J. Immunology.* 1958, Nov., v. 81, No. 5, 389–95, 5 figs. [17 refs.]

The response of 80 pregnant women given poliovaccine in the seventh and eighth months of pregnancy was measured and the decline of antibodies in the infant followed. In addition a group of 62 pregnant women were also studied for the relationship between the maternal and child antibody level. These mothers were inoculated with poliovaccine 6 weeks after delivery. A small group of the infants were inoculated with vaccine at 3 and 4 months of age. The response of the pregnant women to poliovaccine was on the whole rather poor. Only 8 lacked antibody to all 3 types of poliovirus before inoculation and none of these developed antibody to Type 1. The presence of antibody to one type improved the antigenic response not only to that type but also to other types. It was found that the level of antibodies in the mother's serum at the time of delivery, in the cord blood and in the child's blood at 24 hours of age were the same. The rate of decline of antibody passively acquired from a mother was similar for all 3 types and was not affected by whether the antibodies were naturally acquired or acquired as a result of vaccination. If the maternal antibody titre was in the range 1 : 256 or more then almost all infants had detectable antibodies at 3 months of age; on the other hand with maternal titres in the range of 1 : 16 to 1 : 64 most of the infants had antibodies at 2 months of age but more than half lacked them at 3 months. If the maternal antibody level was only 1 : 8 or less the child only rarely had detectable antibodies 1 month after birth.

The results of vaccinating 33 of the infants at 3 and 4 months of age are not presented in detail but in the discussion it is said that the antigenic response in these infants was very poor. It is considered that this may have been due to the poor potency of the particular lot of vaccine used or that it may have been due to a poor response on the part of such young infants or alternatively it may have been due to a blocking effect of passively transferred maternal antibodies. It is said that experiments to test these 3 possibilities are under way. *A. J. Beale*

MONGAN, E. S. **Neurological Symptoms possibly related to Poliomyelitis Immunization.** *U.S. Armed Forces Med. J.* 1958, Nov., v. 9, No. 11, 1659–62.

A nurse aged 25 became ill 3 hours after her second injection of Salk vaccine, given in her left arm 6 weeks after the first injection. Her symptoms were headache and malaise with weakness and pain in the right leg, the lumbar and right gluteal areas: 2 days later weakness of the right arm developed. Superficial and deep reflexes were active and normal: there were no sensory changes and no muscle atrophy. Her temperature on admission was 99·9°F. and reached 99·5°F. for at least some part of the first 20 days in hospital. Cerebrospinal fluid showed 66 mgm. protein per 100 ml. but was otherwise normal: the protein had fallen to 62 mgm. on the 8th day and to 36 mgm. on the 25th day. By the 6th day muscle power began to recover rapidly: by the 8th day the right arm was normal but the leg, although the patient was ambulant, remained weak. The patient's gait was normal by the 45th day though traces of muscle weakness could be detected as late as the 70th day when the patient returned to duty. There was eventually no residual muscle weakness. No precise diagnosis was made but it was felt quite possible that the illness was a neurological complication of immunization. No virological studies appear to have been made. *A. B. Christie*

GEAR, J. & MEASROCH, Veronica. **Cases of Meningo-Encephalitis due to the Coxsackie A-Like Echo 9 Virus.** *South African Med. J.* 1958, Nov. 1, v. 32, No. 44, 1062–6. [16 refs.]

In the years 1955–7 there was a prolonged epidemic of poliomyelitis in South Africa. During this time many cases of suspected non-paralytic poliomyelitis were examined for viruses. From 8 of these patients a virus strain was isolated which produced Coxsackie A type lesions in baby mice, but was serologically ECHO type 9. The 8 patients suffered from meningo-encephalitis indistinguishable from other reported cases of ECHO 9 meningitis. The virus was isolated from the cerebrospinal fluid of 2 of the patients and from the faeces of the others. The virus from 1 patient was isolated in suckling mice, but from all the others virus was first isolated in monkey kidney tissue culture and only subsequently proved pathogenic for suckling mice. The patients came from Johannesburg, Durban and Port Elizabeth, which demonstrates the wide distribution of the virus, although no epidemic was described. There is a brief review of the literature showing the world-wide distribution of ECHO 9 meningitis. The close relationship between ECHO and Coxsackie viruses is noted. *A. J. Beale*

KIBRICK, S. & BENIRSCHKE, K. **Severe Generalized Disease (Encephalohepatomyocarditis) occurring in the Newborn Period and due to Infection with Coxsackie Virus, Group B. Evidence of Intrauterine Infection with this Agent.** *Pediatrics.* Springfield, Ill. 1958, Nov., v. 22, No. 5, 857–75, 10 figs. [41 refs.]

2 fatal cases of neo-natal Coxsackie B4 infection are described in detail. One patient was definitely infected *in utero* and the other possibly. Both mothers suffered from mild febrile illnesses almost certainly due to Coxsackie B4. The virus was recovered from the myocardium of both patients and from the liver and spinal cord of one of them.

Necrotic lesions were found in the myocardium of both patients. The liver was also involved in both, in the first it was enlarged but there was extensive central necrosis (Coxsackie B4 was isolated from the liver but it may have been derived from the heart which was contained in the same vessel). The liver in the second patient showed more extensive disease, it was shrunken, rusty brown and flecked with yellow necrotic areas. One of the features of the illness in this case had been severe haemorrhage. Histological lesions were also found in the central nervous system and pancreas of both patients and the adrenal cortex of the second.

The virus was recovered in monkey kidney cultures and was pathogenic for suckling mice. In suckling mice in addition to the usual B type lesions both strains produced poliomyelitis-like lesions in the central nervous system. The viruses were not recovered initially in cultures of human amnion or renal cells, but later limited cytopathic changes were noted in human amnion cells infected with these viruses.

[The paper includes a good review of the published cases of this serious disease.] *A. J. Beale*

STONES, P. B. **Isolation of E.C.H.O. Virus Type 9 during an Outbreak of Meningo-Encephalitis.** *Brit. Med. J.* 1958, Dec. 20, 1514. [10 refs.]

LYLE [this *Bulletin*, 1957, v. 32, 236] described an outbreak of meningo-encephalitis with a rash in Newton-le-Willows, Lancashire, which occurred in July 1956. 7 faecal specimens from patients involved in this outbreak were examined for viruses and 4 yielded ECHO 9 virus. In addition 8 out of 10 patients from whom paired sera were obtained showed a rise in titre of ECHO 9 neutralizing antibodies. *A. J. Beale*

EDGREN, D. C., PALLADINO, V. S. & ARNOLD, A. **Japanese B and Mumps Encephalitis. A Clinicopathological Report of Simultaneous Outbreaks on the Island of Guam.** *Amer. J. Trop. Med. & Hyg.* 1958, Sept., v. 7, No. 5, 471–80. [10 refs.]

This is a report on the clinical and pathological aspects of the encephalitis outbreak on Guam reported by HAMMON *et al.* [this *Bulletin*, 1959, v. 34, 31]. Onset of the disease was usually sudden in Japanese encephalitis but often gradual in mumps. Coma and convulsions were common in Japanese encephalitis but absent in mumps. Only 2 patients had paralysis and both had Japanese encephalitis. Leucocyte counts and cerebrospinal fluid examinations did not differentiate the 2 types. 4 of the 5 deaths were in proved cases of Japanese encephalitis, and of 4 cases with post-encephalitic symptoms, 2 were Japanese encephalitis and 1 mixed. The pathology of the fatal cases (Japanese encephalitis) showed little gross change in the central nervous system except congestion. Perivascular cuffing was present in all and haemorrhages in the pons of one. Lesions comprising "slight to moderate" neuronal degeneration were commonest in the cord and brain stem and least so in the cerebral cortex.

C. E. Gordon Smith

PIEPER, S. J. L., Jr. & KURLAND, L. T. **Sequelae of Japanese B and Mumps Encephalitis. Recent Follow-up of Patients affected in 1947–1948 Epidemic on Guam.** *Amer. J. Trop. Med. & Hyg.* 1958, Sept., v. 7, No. 5, 481–90. [14 refs.]

This is a follow-up 10 years later of the patients described above. Of 25 who had had Japanese encephalitis with or without mumps, 15 had no sequelae, 8 had neurological or intellectual defects, and 2 had psychiatric defects. Details are given. Sequelae appear to be more severe when the disease is contracted in early childhood. Most patients who had had convulsions, stupor, coma, personality or reflex changes during the acute disease later had sequelae.

Of 11 patients who had had mumps encephalitis only 3 had minimal neurological sequelae. The authors suggest that the lower mortality and higher incidence of sequelae in this outbreak compared with epidemics in Japan may have been due to the high standard of hospital care in Guam which permitted the survival of patients who would otherwise have died.

C. E. Gordon Smith

HAYES, R. O. & DOANE, O. W., Jr. **Primary Record of *Culiseta melanura* biting Man in Nature.** *Mosquito News.* 1958, Sept., v. 18, No. 3, 216–17.

A single instance of attempted feeding on man by *Culiseta melanura*, normally a bird-biter, and vector of eastern equine encephalitis, is described from Massachusetts. *E. R. Nye*

BRAND, C. A. **An Outbreak of Typhoid Fever in St. Lucia (Summer, 1957).** *West Indian Med. J.* 1958, June, v. 7, No. 2, 142–8.

This is an account of 22 sporadic and 97 epidemic cases of typhoid fever occurring during 1957 in St. Lucia. The source of infection was probably the river, which the inhabitants used for drinking water, as well as for laundry and bathing. Phage typing was done in 5 cases and 2 phage types E_1 and C were isolated. The epidemic terminated very rapidly after September.

The disease spared the very young and the elderly. Some 35% of the patients were under 12 years of age and some 65% between 13 and 40. The symptoms were classical in most cases, but about 25% of the cases could be described as mild or abortive; "pea soup" stools and profuse diarrhoea were uncommon; a rash was observed in 50% of the cases. Complications were mainly pulmonary, and no case of perforation or

haemorrhage was recorded. There were 8 deaths—all from toxaemia and dehydration.

Drug treatment was by chloramphenicol 50 mgm./kgm. loading dose and 50 mgm./kgm. daily in divided doses given every 6 hours until the temperature had been normal for 3 days—an average duration of treatment of 7½ days. Only 3 relapses were noted, but some may have been missed owing to the very early discharge of the patients from hospital.

Some 3,500 people were injected with TAB vaccine during the epidemic. 19 cases of typhoid fever were discovered shortly after the first or second injection of TAB; but 5 of these occurred 2 weeks after the second injection, and 2 even later. It is considered that immunity may be slow to develop in some people after TAB vaccine, and that a third injection might be of advantage. *H. Stanley Banks*

O'Connor, Mary E. **Efficacy of Chloramphenicol Therapy for Typhoid Carriers.** *Pub. Health Rep.* Wash. 1958, Nov., v. 73, No. 11, 1039–50. [29 refs.]

The study reported here was carried out in the attempt to answer the question of whether chloramphenicol therapy in typhoid fever has any effect in the prevention of the chronic typhoid carrier state. Data were collected of 1,413 cases of typhoid fever which occurred in Mississippi and Louisiana in the period 1947–1952 from morbidity, mortality, laboratory, epidemiological and hospital reports; from physicians and pharmacists; and by personal investigation during 3 years. The study population was divided into 4 groups: (1) those patients who received no chloramphenicol, (2) those receiving inadequate total dosage of chloramphenicol, (3) those who received an adequate treatment with a total dosage (30 gm. or over) of the drug initiated before the 15th day of the disease and (4) those treated with an adequate dosage begun after the 15th day of the disease. The data are described and set out in tables which give: (1) the number of patients in the 2 states by age, race, sex and population attack rate, (2) distribution of cases by diagnostic criteria and type of treatment, (3) distribution of accepted cases by time of collection of first negative faecal specimen and by method of treatment, and (4) relation of age, sex and treatment to the development of the carrier state.

The general picture and statistics of typhoid fever as seen in these 1,413 cases of which 614 formed the control group, are recorded in the summary but the main point which emerged in regard to the purpose of the study was "Although early adequate treatment with chloramphenicol appeared to hasten the termination of excretion of *S. typhi* in many cases, evidence that early treatment acted to prevent the chronic carrier state is weak. The carrier rate for all patients treated with chloramphenicol was 1·0 percent and that of the nonspecifically treated group was 2·0 percent". *M. E. Delafield*

Sommerville, R. G., with the technical assistance of H. G. Carson. **Enteroviruses and Diarrhoea in Young Persons.** *Lancet.* 1958, Dec. 27, 1347–9, 1 fig.

Previous work has shown that enteroviruses, which comprise the polio, Coxsackie A and B and ECHO groups of viruses, are quite frequently found in the stools of healthy children. Eichenwald *et al.* [this *Bulletin*, 1958, v. 33, 734] have shown that ECHO virus type 18 can cause outbreaks of diarrhoea in young children. Also Ramos-Alvarez and Sabin [*ibid.*, 1958, v. 33, 1115] have described suggestive evidence that other members of the enterovirus family may be the aetiological agents of some cases of diarrhoea.

Sommerville studied the incidence of enteroviruses among children admitted to the Ruchill Hospital, Glasgow, with gastroenteritis or dysentery and among a control group of children admitted to the same hospital with a diagnosis of respiratory disease. All the children were under 5 years of age and were studied during the year starting April 1957. Stool samples were tested for enteroviruses by inoculation of cynomolgus monkey kidney cultures. Any cytopathic agent was identified by means of poliovirus antisera Types 1, 2 and 3, Coxsackie virus types B 1 to 5 and A 9 and ECHO viruses 1 to 14 [the ECHO virus group has had some additions since this work was performed]. 338 children with diarrhoea and 115 with respiratory symptoms were studied. However, no patient was admitted with respiratory disease until September 1957 and so comparisons have been made for the 7-month period from September 1957 to the end of March 1958 and in this period 223 patients with diarrhoea were admitted to the hospital.

The total isolation rate was 14% for the control group and 21% for the patients with diarrhoea. There was no significant difference between the isolation rates of the 2 groups of patients for any of the identifiable enteroviruses. However, 9 unidentified agents were isolated from the group of children with diarrhoea. These agents could not be identified by means of the ECHO sera available but it is at least possible that they are really members of the same group of agents that remain to be assigned to their proper serological type. The identified virus most frequently isolated was ECHO virus type 7.

In addition to the virus studies bacteriological examinations were undertaken of all stools from the patients with diarrhoea. It was found that the incidence of pathogenic *Escherichia coli* was highest in the children under 1 year and that the incidence of *Shigella sonnei* increased until it reached the highest level in the 3–5-year-old children. There was very little difference in the isolation rate for enteroviruses with age although the children under 2 had a slightly higher isolation rate than the children between 3 and 5 years of age. Quite commonly both a pathogenic bacterium and a virus were isolated from the same specimen, the most frequent combinations being between *Sh. sonnei* and ECHO 7 and *Sh. sonnei* and Coxsackie A 9. From the data presented it is not possible to ascribe an aetiological role to any of the viruses isolated in this study. The author, however, is continuing his survey and hopes to supplement it with antibody studies and also with attempts to identify the agents that have so far proved untypable with the range of antisera at present available. *A. J. Beale*

ARMSTRONG, J. G. **Acute Gastroenteritis. A Review of 821 Cases treated at the Hospital for Sick Children during the Year 1956.** *J. Pediatrics.* St. Louis. 1958, Dec., v. 53, No. 6, 704–18, 7 figs.

The purpose of the study of acute gastroenteritis described in this paper was to "attempt to appraise advances that have been made and to gauge the relative importance of various etiologic agents in gastroenteritis". The patients studied consisted of 821 children of all ages who were admitted for gastroenteritis to the Hospital for Sick Children in Toronto throughout 1956 or who developed the disease during their stay in hospital. Out of this total only children under the age of 2 years were studied in detail and of these there were 641 (78%).

A table sets out a classification of the disease in these patients: Group I. "Usual flora" reported from stool culture and no evidence of disease other than gastroenteritis, 293 patients (46%); Group II A. "Usual flora" but suffering from pyogenic infection outside the gastrointestinal tract—this group is termed "parenteral gastroenteritis", 104 patients (15·9%); Group II B. No stool culture obtained—mostly "parenteral gastroenteritis" secondary to clinical upper respiratory tract infection, 27 patients (4·2%); Group II C. Accepted pathogenic bacteria cultured from the stool: *i.e. Salmonella, Shigella* and pathogenic *E. coli* groups, 51 patients (7·9%); Group II D. Organisms of debatable pathogenicity isolated from stools: *i.e. Proteus, Pseudomonas, Paracolobactrum,* streptococci, *Bacterium anitratum* and Providence group, 100 patients (15·7%); and Group II E. Pyogenic staphylococci isolated from stools, 66 patients (10·3%).

There is a detailed analysis of seasonal incidence, age incidence and mortality and comparison of the findings with those recorded by WOLFISH (*J. Pediatrics*, 1953, v. 43, 675) for 1951 and 1952. Mortality from gastroenteritis in this hospital which was between 40 and 50% before 1930 fell to 3·3% in the 1952 series and was 0·97% in 1956. Among other conclusions are: seasonal incidence is now greatest in January and February instead of during the autumn and only in infants below the age of 3 months is it greatest in the autumn; evidence is produced that *Proteus vulgaris* may be a pathogenic organism and hospital cross-infection with pathogenic *E. coli* has been virtually eliminated as the result of isolation of all patients and the investigation of more patients by stool culture. *M. E. Delafield*

TUBERCULOSIS

LAUGWITZ, N. & MIELSCH, W. Arbeits- und Versicherungsschutz im tuberkuloseverseuchten Rinderstall. **[Protection and Insurance for Workers in Contact with Tuberculous Cattle]** *Ztschr. f. ärztl. Fortbildung.* 1958, July 15, v. 52, No. 14, 601–4. [11 refs.]

There are 3·7 million cattle in the East German Republic, of which about 1 million are tuberculin reactors. It is estimated that there are 60,000 infectious animals throughout the country compared with about 52,000 human infectors. The incidence of the disease is excessively high in milk cattle and workers in contact with them undergo as much risk of infection as do workers in the health service who attend tuberculous patients.

The regulations which protect workers cover only those in hospitals and pathological and bacteriological laboratories. They do not extend to persons working with cattle.

It is advisable that all persons working in a tuberculous environment should be tuberculin reactors. This can be achieved easily by BCG vaccination which vaccination should be extended widely and even made compulsory for all young non-reactors working with cattle. Moreover routine X-ray examination should be introduced and workers should be adequately instructed about the danger of infection.

Various preventive measures have been recommended including compulsory notification of tuberculous animals to the local medical officer of health. Whether compulsion be adopted or not the discovery that a cow is a reactor should lead to full investigation of its bovine and human environment. Cooperation between veterinarian and tuberculosis physician should be improved so that, for example, when a reactor appears in the herd the presence of a human infector is not lost sight of or when a patient is found to have cervical adenitis the possibility of an infector in the herd is not missed.

Tuberculosis as an occupational disease is then discussed, and in this context the authors emphasize that more attention must be paid to accurate typing of the tubercle bacillus in every case. An example is given of a claim for industrial injury benefit being disallowed because the tubercle bacillus found in the patient (a dairy worker) was of the human type. Possible arguments against this decision are listed, *viz.* double infection (possible), change of type (impossible except after years of culture passage), error in typing, exacerbation of old foci of human disease due to super-infection by bovine bacilli (possible) and infection by human bacilli from cattle (possible but highly improbable).

It is not yet certain that tuberculosis due to a bovine strain of the organism can be expected solely on the grounds of occupational exposure to infection, and intensive research on this question is necessary. There is, however, no doubt that tuberculosis is an occupational disease. *H. G. Calwell*

SITA-LUMSDEN, E. G., KLEIN, Dorothy I. & LOGAN, J. S. **Tuberculosis in a Grammar School.** *Med. Officer.* 1958, Dec. 26, v. 100, No. 26, 395–7.

In 1954 and again in 1955 an unexplained case of tuberculosis had occurred among children attending a boys' school in Essex, England. A tuberculin survey had not disclosed an excessive reactor rate and X-ray examination had not disclosed other cases of the disease.

In March 1956 another pupil was found to have tuberculosis but in view of the earlier negative findings a source of infection within the school was not suspected.

In April 1956 3 other pupils were found to have tuberculosis (pleural effusion 1, inactive primary tuberculosis 1 and primary tuberculosis 1). Before a full

investigation had been begun another pupil was found to have tuberculosis.

Tuberculin testing of the pupils was begun at the end of May and all members of the staff were urged to submit to X-ray examination, which began in mid-June at which time notification was received that a pupil was ill with tuberculous meningitis. A teacher was found to have active pulmonary tuberculosis and was admitted to hospital.

After X-ray examination of the reactor pupils 3 other cases of primary tuberculosis were notified, and on review of their histories 2 pupils who had previously attended the chest clinic were reclassified as tuberculous. 5 other boys were placed under supervision, one of whom gave a history of erythema nodosum in January 1956. A second teacher was also notified as having non-infectious tuberculosis.

It was considered highly probable that this outbreak was due to the reactivation of the teacher's healed tuberculous lesion in late middle-life. Some 18 months earlier he had been examined by a consultant physician who had not detected activity of the disease. The infectious state was thought to have supervened in the autumn of 1955.

Details of the results of the tuberculin tests are given by classes. Disproportionately high reactor rates were found in 2 classes taught by the infector teacher, and even if he had refused X-ray examination he would have been detected because of the large number of reactors among the pupils in contact with him.

In September 1957 a former pupil, who had shown a high degree of tuberculin sensitivity when examined at school in June 1956, was found to have pulmonary tuberculosis with cavitation. The infector died after a thoracic operation.

The authors do not recommend annual X-ray examination of all school teachers as "it is questionable in the present state of our knowledge whether one would be justified in imposing this additional radiation burden in an unselective way". They propose X-ray examination of all entrants to the education service, the scrutiny by a doctor of all sickness certificates and annual X-ray examination of male teachers after the age of 55. [As far as the reviewer is aware it is still the recommendation of the Joint Tuberculosis Council that persons whose employment brings them into close contact with groups of children should have an X-ray examination of the chest *annually*.]

H. G. Calwell

WOOD, L. E., FURCOLOW, M. L. & WILLIS, M. J. **An Evaluation of Tuberculosis Case Finding by Tuberculin Testing and Some Observations of Histoplasmin Sensitivity among Young School Children.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 667–81, 3 figs.

This work was done in Kansas, Missouri, U.S.A., in the years 1947–57. During the last 7 years of the period not only were children in the kindergarten tested with tuberculin and histoplasmin but those of them who did not react were re-tested in the following year. All reactors had their chests X-rayed and contacts were invited to come for X-ray examination.

The tuberculin used was PPD, 5 TU and the histoplasmin was a 1 : 100 dilution. During the period 66,033 tests were done on 51,040 children.

The tuberculin reactor rate in white children varied irregularly from 0·7% to 2·6% (overall rate 1·5%), and in Negro children from 3·8% to 1·7% (overall rate 2·6%). The histoplasmin reactor rate for the entire white group was 10·4% and for the Negro children 8·7%. The tuberculin sensitivity rate showed no tendency to decline over the entire 10-year period whereas the histoplasmin reactor rate tended to decrease in white and to increase in Negro children.

The tuberculin conversion rate in 1950–7 (between kindergarten and first grade) was 1·0% in white and 1·4% in Negro children. There was no tendency for the rate to fall during the period of observation. The histoplasmin conversion rates were consistently higher in Negro than in white children, being 4·7% and 2·6% overall respectively.

There was a close relationship between tuberculin reactor rates and tuberculosis mortality rates for the white population.

The yield of active tuberculosis among the contacts of original reactor and convertor children was: new 1·2%, already known 3·6%. Approximately 6 contacts were examined for each convertor and 4½ for each original reactor so that 4,663 adult and child contacts were examined. The discovery rate of new cases was essentially the same in the white and Negro groups but that of already known cases in the Negro group was almost twice that in the white group.

The yield of new active tuberculosis was twice as high among household as among non-household contacts (1·4% compared with 0·8%). The discovery rate was directly proportional to the size of the tuberculin reaction in the index child; 30 times as much tuberculosis was found among the contacts of children with more than 25 mm. of induration as among those whose reactions measured 5–9 mm.

No information is given about tuberculosis discovered in the reactor children themselves except that the yield was low "as would be expected".

The discovery rate of new active tuberculosis in the contacts was 12 times that obtained by mass radiography and in addition active disease was found in many known patients in whom the disease had been considered inactive.

The failure of the tuberculin reactor rate to decline in the 10-year period is discussed. The possibility of its inflation by the presence of non-specific sensitivity is mentioned.

H. G. Calwell

KUNOFSKY, S. & KATZ, J. **The Stability of the Tuberculin Reaction.** *Amer. Rev. Tuberculosis.* 1958, Dec., v. 78, No. 6, 862–70, 1 fig.

This study of tuberculin sensitivity was made in 2 schools for mental defectives in New York State between 1936 and 1952. In the first school all persons attending were tested at the beginning of the study or on admission and non-reactors were retested every 6 months. Original reactors were not retested but original non-reactors who underwent conversion were

retested every 6 months until 1948. Owing to failure to preserve the records of this work complete information was available for only 411 original non-reactors representing about 10% of the total number in the original study. The tuberculin test used was Mantoux with 0·00025 mgm. of PPD, and any recognizable induration was considered to be evidence of sensitivity.

In the second school tests were done in 1948 as part of the BCG vaccination programme. The preliminary test used 0·00002 mgm. of PPD and non-reactors to this dose were then given 0·005 mgm. The criterion of a positive reaction was induration of 5 mm. or more. All the original reactors, numbering 1,992, were retested twice in 1951 and in 1952. The shortest period between first and last tests was 2½ years. In order to remove the effect of error in reading weak reactions, emphasis in the study was placed mainly on the changes seen among those with reactions of 10 mm. and over.

In the first group all became reactors at some time or other during the period of the study but 41% failed to react on occasion and 15% were negative at the end of the observation period. Similar variations were found at all levels of sensitivity. The degree of sensitivity did not remain static after reaching its peak but tended to decrease with time. For example 20 (38%) of 53 persons with reactions showing necrosis of the skin later reverted to negative and 50 (45%) of 112 with reactions of over 20 mm. also reverted. While 13% of the original non-reactors developed the highest degree of sensitivity at some time, only 3% showed this degree at the end of the study. Conversion, reversion and again conversion were found to occur.

All of the 1,992 persons in the second group were reactors on admission to the school. Among reactors to first strength PPD 8% with reactions of 20 mm. or more, 16% with reactions of 10–20 mm. and 44% with reactions up to 10 mm. were found to have reverted when retested with the same dose of PPD and 4, 3 and 12% respectively were found not to react to second strength PPD. Reversion was much more frequent among those with low sensitivity and least frequent in those with high.

The change in sensitivity was sometimes towards increase. For example almost 8% of those responding to first strength PPD with reactions of 10–20 mm. at the initial test reacted later with over 20 mm. of induration, while in 30% the last response was weaker than the first.

One factor contributing to the weakening or disappearance of tuberculin sensitivity was change in exposure to tuberculous infection. Conversion rates tended to increase with increased exposure and reversion rates to decrease with decreased exposure. The concept of the constancy of tuberculin sensitivity may have arisen when infectious tuberculosis was much more prevalent than at present, and with a falling incidence of the disease reversion may become more important.

H. G. Calwell

MARKS, R. H., TOKUYAMA, G. & PETERSON, Agnes. **A Five-Year Pilot Study of Tuberculin Testing in Honolulu Schools. Progress Report of the First Two Years of Observation.** *Amer. Rev. Tuberculosis.* 1958, Dec., v. 78, No. 6, 871–83, 3 figs.

A 5-year tuberculin survey was begun in the schools of Honolulu in 1955 to include 23,000 of the 97,000 school population of the island of Oahu on which the city is situated. The Mantoux test was used with 10 TU of PPD.

In the first year 22,958 children (94%) were tested and 1,666 (7·3%) reacted with induration of 6 mm. or more. During the second year 23,993 (92%) were tested and 1,892 (7·9%) reacted.

Analysis of the results by race showed that of the major racial groups the Japanese appeared to have the lowest reactor rates (males 5·7%, females 4·7%) and the Filipinos the highest (14·5 and 12·0% respectively). Analysis by age and sex showed that there was a sharp rise in the rate in males after the age of 14 and in females at 17. The rates were considered to be higher than those in comparable groups in continental U.S.A.

During 2 full years of the project 8 of 1,912 reactors to 10 TU were discovered to have active pulmonary tuberculosis (new cases), an incidence of 0·3 per 1,000 children tested.

The yield of new cases of active disease in 9,625 household contacts of reactor children was 0·9/1,000 for all ages. All of the 9 new cases thus discovered were found by examining 2,330 persons aged 15 years and over who were household associates of children whose reactions had measured 8 mm. or more. The yield in this group was 3·9/1,000.

During the first year the criterion of a positive reaction was induration of 6 mm. or more. Of the 1,666 who reacted by this criterion 47% had induration of 6–7 mm. The authors believe that such reactions are more probably non-specific than due to tuberculous infection. If the criterion of a positive reaction had been raised to 8 mm. or more the reactor rate would have been 4·8% instead of 7·3%. No new cases of tuberculosis were discovered in the contacts of children with weak reactions (6–7 mm.). In the third year of the survey the criterion of a positive reaction was raised to 8 mm.

Rates of conversion and reversion were studied by testing each child each year regardless of his reaction the previous year. Of the 17,297 children tested in both years who had no reaction or reactions of 5 mm. or less in the first year 691 had reactions of 5 mm. or more in the second year, a conversion rate of 4·0%. The reversion rate in this group was 26·4%. Of the 17,849 children who had no reaction or reactions of less than 8 mm. in the first year 272 had reactions of 8 mm. or more in the second year, a conversion rate of 1·5%. The reversion rate was 12·4%.

The authors were impressed with the relative inexactness of the tuberculin reaction as a means of separating the population studied into those infected with the tubercle bacillus and those not so infected. Mention is also made of the difficulty of achieving accurate technique and of determining the presence or absence of induration and measuring it to within 1 mm. They advise that with the test dose of 10 TU and the technique used in this study the criterion of a positive

reaction in such a survey should be induration of not less than 8 mm. *H. G. Calwell*

SINDO, T., UTAHASHI, T., HAGA, K., HIYAMA, A. & ITOI, M. **Further Studies on Patterns of Hemolytic Test in Tuberculosis using Serum Samples of Tuberculous Patients and Healthy Persons in Japan, with special reference to relationship between Results of Hemolytic Test and Tuberculin Skin Test on Healthy Persons.** *Japanese J. Tuberculosis.* 1958, June, v. 6, No. 2, 61–74, 14 figs. [10 refs.]

In these investigations the haemolytic titres of the sera were measured in the presence of 0·5, 1, 2 and 4 units of complement with red cells sensitized with an antigen, which had been extracted from tuberculin with phenol and precipitated with ethanol. The haemagglutination tests were made with the cells sensitized with this same antigen, and the tuberculin tests were done with 1 : 2,000 OT, diameters of redness of less than 0·5 cm. being regarded as negative, of 0·6–0·9 cm. as false positive and of 1·0 cm. or more as positive. [These measurements are wrongly shown as mm. in the original.]

The results of the *in vitro* tests on 72 sera from tuberculous adult patients show that there was no close relationship between agglutination and haemolytic reactions with 4 units of complement; 4 cases gave positive agglutination reactions but negative haemolytic reaction, in 5 the results were the reverse and in 4 they were negative by both methods. In general, the titre of the agglutination test was higher in the moderately advanced cases than in either the minimal or the advanced cases, but the haemolytic titre tended to be lowest in the mild cases. With these sera the pattern of the haemolytic titres, *i.e.* the fall in titre which occurs with the lesser quantities of complement, was very variable.

Attempts were made to relate the tuberculin reaction with the haemolytic pattern of 148 clinically healthy adults but only partial parallelism was found; of 54 tuberculin positive reactors 39 gave positive haemolytic reactions, and of 68 false positive tuberculin reactors 48 gave positive haemolytic reactions, and of 26 negative reactors 15 gave positive haemolytic reactions. In general, the fall in the haemolytic titres with the decreases in the complement was greater than in the tuberculous sera and some sera showed a prozone effect. A similar examination was made on 414 healthy children, aged 8–12 years, from a primary school in Tokyo City; 108 of the children were tuberculin-positive, 178 were false positive reactors and 128 were negative. In these children there was again only partial correlation between the tuberculin reaction and the haemolytic titre but in general the haemolytic titres were lower than in the adults. *S. R. M. Bushby*

OSHIMA, S., FUJITA, Y., TAKEOKA, A., NAKAJIMA, M. & TSUJI, S. **Chemical Analysis of the Role of Humoral Factors in Native and Acquired Resistance to Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, Dec., v. 78, No. 6, 884–98, 1 fig. [29 refs.]

STRADLING, P. & DIXON, W. M. **Possible Disadvantages of a Chest Radiography Service for General Practitioners.** *Brit. Med. J.* 1958, Dec. 6, 1383–5.

There has been considerable controversy about the value and dangers of a chest X-ray service for general practitioners and this article goes a long way toward providing an answer.

All patients X-rayed at a general practitioner's X-ray service clinic during the period October 1956 to May 1957 inclusive (673) were considered. 74 of these whose birthday was in May were fully examined clinically; 56 patients were radiologically normal. Of these 4 were found to be clinically abnormal: 1 chronic bronchitis with an exacerbation, 2 had minor skeletal deformities not requiring treatment.

Of those patients whose birthdays fell in November, by a coincidence also 74, 63 had normal miniature films. Their doctors were written to to establish their fate. Of 61 patients 48 recovered rapidly from the complaint which had prompted the X-ray. In the other 12, 8 had bronchitis with or without asthma, 4 had extra-thoracic disease: hepatitis, hypochromic anaemia, alcoholic dyspepsia and gout. 1 had fractured ribs which were not visible on the miniature film, even on rescrutiny. None of the 61 patients developed significant chest disease during the following 8 months: 1 patient developed caval obstruction due to a carcinoma of the bronchus, but it is thought that this was unrelated to the original symptoms.

It is obviously advantageous that the clinical examination and care should remain in the hands of the general practitioner unless it prejudices the patient. The survey shows no evidence of this, and will encourage the establishment of further general practitioner X-ray services. *F. H. Young*

KALTHOFEN, A., VAN VLIET, B. & VAN DER ZEE, J. **Second Chest X-ray Survey of the Population of Amsterdam.** *Acta Tuberculosea Scandinavica.* 1958, v. 36, Nos. 2/3, 141–51.

A mass radiography survey was carried out in Amsterdam (population 871,188) during the period June 1954 to August 1957, the aim of which was to include all persons of 14 years and over. A similar survey had been made between April 1951 and May 1954. The total number examined was 400,959, which was 76·3% of the potential number. Of this total 178,979 (44%) were males and 221,980 (56%) were females.

6,772 persons were called to the Tuberculosis Centre for further examination, and the discovery rate of active pulmonary tuberculosis was 0·45 per 1,000 of the total population compared with 0·92 per 1,000 in the 1951–4 survey. The decrease in incidence in males was 52% and in females 65%.

In the 179 cases discovered the disease was of moderate severity in 68, severe in 4 and mild in 107. Cavitation was present in 53 (30%) compared with 71 (19%) in the earlier survey. The sputum was positive for tubercle bacilli on direct examination in 46 patients

and positive cultures were obtained from 75. The percentage of sputum-positive patients was therefore 67 compared with 58 in 222 patients earlier.

Sanatorium or hospital treatment was accepted by 141 patients and declined by 28, who were therefore treated at home. It was considered that the disease was fresh in 127 patients and that 52 had suffered relapse.

As in the first survey there was a predominance of male patients, 113: 66, although the number of females examined exceeded that of males by 43,001. The highest incidence of active tuberculosis was found in the 32,967 males aged 40–49 (0·93 per 1,000) and the lowest in the 36,620 females aged 50–59 years (0·13 per 1,000).

Inactive pulmonary tuberculosis was found in 4·9% compared with 4·5% in the earlier survey, and lung tumours were found in 185 patients, which were malignant in 135. 24 males were submitted to surgical operation with good result. There was a favourable operative condition in 25% compared with only 9·6% in the earlier group. In the 96,651 males over 40 years of age there were only 62 with active pulmonary tuberculosis but there were 92 with bronchial carcinoma, 66 of whom were heavy smokers of cigarettes and 11 moderately heavy smokers. The smoking habits of 15 were not known. *H. G. Calwell*

KIMSEY, Letitia S. **The Bacteriological Diagnosis of Childhood Tuberculosis using Bone Marrow and Peripheral Blood Aspirates.** *J. Pediatrics.* St. Louis. 1958, Oct., v. 53, No. 4, 413–31. [31 refs.]

Following the suggestion of KATZ *et al.* (*Med. Clin. North America,* 1950, Nov., 1817), the authors aspirated the marrow from the upper end of the tibia of patients under 2 years old and from the iliac crest of other patients. The marrow was diluted in Hanks solution, centrifuged, and the smears, the cultures on Löwenstein-Jensen medium and the inoculations of the guineapig were made from the deposit. Similar examinations were made on the peripheral blood after the red cells had been lysed by adding 5 ml. of the citrated blood to 30 ml. of 3% acetic acid and the deposit washed in distilled water. The results on 30 patients are described, the patients being divided into 3 series.

Series I was composed of 13 patients who had a definite diagnosis of tuberculosis without accompanying meningitis. Marrow smears were found positive in 5 of these patients, 2 of them being also positive both by culture and guineapig inoculation, and positive blood smears were obtained from 7, tubercle bacilli being isolated from 2 of them. Miliary tuberculosis was the final diagnosis in 1 of these children.

Series II consisted of 11 patients in whom the diagnosis of miliary tuberculosis had been established; marrow smears were positive in 8 of these patients and 5 were positive by culture and guineapig inoculation. Acid-fast bacilli were also present in the blood smears of these 5 patients but tubercle bacilli were not isolated. Miliary tuberculosis was finally diagnosed in 8 of these patients.

Series III consisted of 6 patients for whom the final diagnosis was not tuberculosis, and acid-fast bacilli were not demonstrated in any of them.

The principal value of these examinations is in the diagnosis of miliary tuberculosis, for, of the 9 patients in whom this was the final diagnosis, positive marrow smears were obtained in 8, the bacilli being isolated from 6, and positive blood smears were obtained from 6. The patients from whom no bacilli were detected in smears and those from whom the bacilli were not isolated, had been given treatment with antituberculous drugs for at least a week.

The failure to isolate the bacilli from the other tuberculous patients in spite of there being acid-fast bacilli in the smears, could in some cases have been due to chemotherapy but in others this could not have been responsible, and in these the failure was attributed to such factors as heating during centrifuging, the centrifuging, the scantiness of the bacilli in the inocula, or perhaps a too high concentration of malachite green in the medium.

3 of the cases are reviewed in detail.

S. R. M. Bushby

BREUER, J., ABELES, H., CHAVES, A. D. & ROBINS, A. B. **Observations on Ambulatory Tuberculous Patients with Pulmonary Cavities and Non-infectious Sputum (the "Open-Negative" Syndrome).** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 725–34.

Great interest is being shown in the so called "open-healing" of cavities: of necessity the reports have been on short term follow-up or pathological features. This paper deals with 94 patients who were treated mainly as ambulatory cases and on whom surgery was not performed. The patients underwent a minimum of 6 months' drug therapy, though there is a lack of uniformity. The disease was stated to be advanced in most cases. 6 patients relapsed in the first, 3 in the second and 1 in the third post-treatment year as judged by the reversion of sputum or extensions in the non-cavitary component of the disease. In 9 out of the 10 drug therapy was still being prescribed (though not necessarily taken). Usually, freedom from relapse was associated with large and thin walled cavities. Variations in the appearance of the cavities suggesting bronchial obstruction was common, but had little effect on the relapse rate as defined above. The authors conclude that the prognosis of thin walled cavity cases is sufficiently good to justify an expectant attitude, but where the cavities are thick walled surgery is indicated. This is an interesting paper, but the lack of uniformity of treatment does not allow it to be accepted as authoritative. *F. H. Young*

AMERICAN TRUDEAU SOC. **Antimicrobial Therapy of Tuberculosis. A Statement of the Committee on Therapy.** [BARCLAY, W. R., Chairman]. *Amer. Rev. Tuberculosis.* 1958, Oct., v. 78, No. 4, 656–8.

This statement is in itself a summary, and as such it is impossible to abstract. The most important conclusions are: Streptomycin is most effective if given

daily in 1 gm. doses, but carries with it an increased risk of ototoxicity especially in the older age groups; isoniazid is more effective in combination with one or more of the other drugs and it is unwise normally to use it by itself; some patients acetylate it quickly, and in these higher doses than the usual 300 mgm. daily may be tried; various preparations of PAS give somewhat different concentrations in blood serum; streptovaracin, kanamycin and thiocarbanidin should only be used when experimental control is available.

F. H. Young

BERTE, S. J., DEWLETT, H. J. & SCHMIDT, H. W. **An Evaluation of Chemotherapy in Pulmonary Tuberculosis. Part I: High Doses of Isoniazid with PAS and Pyridoxine.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 773–784. **Part II: Daily Streptomycin Plus High Doses of Isoniazid with PAS and Pyridoxine.** *Ibid.*, 779–84.

This article reports the effect of high doses of isoniazid. 117 cases of pulmonary tuberculosis were treated, but 33 had to be excluded for various causes, leaving a total of 84. Of these 35 had had no previous treatment and 49 had had less than 2 months. In the investigation 37 patients without cavities received 10 mgm. isoniazid per kgm. per day; 40 with cavities received 16 mgm. 7 who showed an inadequate concentration of isoniazid in the serum received 18 mgm. per day. All, in addition, received 100 mgm. of pyridoxine, and 12 gm. of PAS daily. In 64 patients the concentration of free isoniazid in the serum 6 hours after one-third of the daily dose of isoniazid had been given was examined; 25% had 0·3–0·8 μgm. per ml. of serum, and 75% had 1·0–6·5 μgm. Of the 84 patients, 23·8% were sputum-negative on admission; after 2 months' treatment 83·3% were negative, and the percentage gradually rose until at the end of 8 months 100% were negative for tubercle bacilli on culture. As might be expected, the more advanced cases took the longest time to become negative. Of 47 patients with cavities, 58·4% closed their cavities by the end of 6 months. No additional cavity closure was obtained after 8 months' treatment.

I. Using the 700 patients reported by LIVINGS (Fifteenth Conference on the Chemotherapy of Tuberculosis, Veterans Administration) who were treated by 300 mgm. isoniazid daily, as a control, the authors found that tubercle bacilli disappeared from the sputum in 15–20% more cases when a high dose was used than when patients were treated with the standard dose. Closure of cavities up to 4 cm. in diameter was enhanced from 8 to 16%. The adequate serum concentration of free isoniazid seems to be not less than 0·8 μgm. per ml., and 75% of patients achieved this.

II. 77 patients were treated with streptomycin, 1 gm. daily, in addition to the above. 7 had to be excluded for various reasons, leaving 70. The streptomycin was given for 90 days. It was found that little advantage was received as regards sputum conversion between the 2 regimes, and the same applied to radiographic improvement. The rate of cavity closure was a little higher in the streptomycin group. The figures are too small to furnish proof that the addition of streptomycin is of appreciable advantage, though they do suggest that the prospect of cavity closure is enhanced.

The 2 investigations are interesting, as they do suggest that important results can be obtained from high dosage of isoniazid, and this improvement is more striking than has been reported by some other workers. The investigation appears to have been carefully controlled, but the numbers are too small to do more than indicate a trend. *F. H. Young*

BRIDGE, E. V. & CARR, D. T. **Clinical Use of a Single Daily Dose of Para-Aminosalicylic Acid in association with Isoniazid.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 749–52.

The disadvantage of para-aminosalicylic acid as a drug in the treatment of pulmonary tuberculosis lies largely in its irritant effect on the gastrointestinal tract. Experimental evidence drawn from guineapigs suggests that the efficiency of a single daily dose of 7 gm. of calcium or potassium para-aminosalicylic acid (5 gm. PAS) is comparable with the usual dosage. As this dosage has been reported as causing less gastrointestinal disturbance the authors tried the regime combined with isoniazid on 70 patients, of whom for one reason or another, 47 were available for analysis. Intolerance was shown in only 3 of the 47 patients. After 120 days 42 patients had negative sputum cultures. Of the remaining 5, 3 were resistant to isoniazid, and 2 to PAS. Marked radiological improvement was noted in 25 patients, minimal improvement in 8 and no change in 14 patients. The authors use the figures quoted by BOWERMAN at the 16th Conference on Chemotherapy of Tuberculosis as a control, and conclude that the results are equal to those obtained by the use of 10 to 12 gm. para-aminosalicylic daily in divided doses. A case is made out for further study of the single dose regime. *F. H. Young*

KARSLON, A. G. & CARR, D. T. **Effect of Single and of Double Daily Doses of Para-Aminosalicylic Acid in Tuberculosis of Guinea Pigs.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 753–9, 2 figs.

2 experiments on guineapigs were undertaken to determine whether single doses of PAS gave as good results as multiple doses. (1) 40 guineapigs were injected with tubercle bacilli, of these 10 were used as controls, and 5 groups of 6 each were treated with various amounts of PAS, some given daily and some twice a day, subcutaneously. No difference was noted in the results between the effect of the drug given once or twice a day. (2) 38 guineapigs were injected in a similar way, 6 were retained as pretreatment controls. The remaining 32 were divided into 4 groups of 8 animals; 1 group was used as a control. 1 group was treated by 200 mgm. of para-aminosalicylic acid orally daily, a second group with 200 mgm. 3 days a week, and a third with 100 mgm. twice daily 3 days a week. The results were better with the 200 mgm. daily regime than in the regimes when the drug was given 3 times a week, but no advantage accrued from dividing the dose.

Limited studies on the concentration of para-aminosalicylic in the blood suggest that a constant concentration in the blood is unnecessary. *F. H. Young*

ESPERSEN, E. **Goitre and Myxoedema during Treatment of Pulmonary Tuberculosis with Para-Aminosalicylic Acid. Review of the Literature and Report of Three Cases.** *Acta Tuberculosea Scandinavica.* 1958, v. 36, Nos. 2/3, 110–19, 4 figs. [22 refs.]

SHIELDS, T. W., LEES, W. M. & FOX, R. T. **Pneumonectomy in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, Dec., v. 78, No. 6, 822–31, 1 fig.

Resection of lung tissue as a method of treatment has largely taken the place of surgical collapse therapy; but although segmental resections are usually performed without incident, this is not the case when removal of larger amounts of lung tissue, especially pneumonectomy, is undertaken in the average chest hospital.

This article reports the results of 101 pneumonectomies on patients suffering from pulmonary tuberculosis. After a follow-up of 2 to 7 years, 69 patients are alive, 65 with inactive disease. The 60-day mortality was 10·8%, 14 patients have died subsequently, and 7 were lost sight of.

Cardio-respiratory failure was responsible for 6, and haemorrhage for 2 of the hospital deaths. Of those dying later, contralateral spread and complications arising from the bronchial stump were most important. The authors advise thoracoplasty when the histological examination of the bronchial stump shows evidence of active tuberculosis, and when there is any suggestion that infection of the space fluid is impending. Unfortunately routine examination of the sensitivity of the bacilli was not undertaken, but the history of previous antibiotic treatment leads the authors to consider that many patients carried resistant organisms.

F. H. Young

ZINNEMAN, H. H. & TUCKER, W. B. **Seven-to Eleven-Year Follow-Up Study of the Results of Primary Thoracoplasty for Pulmonary Tuberculosis. The Relationship of certain Variables of the Disease to Outcome.** *Amer. Rev. Tuberculosis.* 1958, Dec., v. 78, No. 6, 832–8, 1 fig. [12 refs.]

A large number of papers have been published during recent years on the results of primary thoracoplasty in pulmonary tuberculosis, many of them reporting excellent results. This paper is more pessimistic. The authors think that the relatively poor results they report are mainly due to the fact that they insist on negative pre-discharge cultures (at least 6 sputa and 3 gastric washings were cultured), and repeated negative cultures during the follow-up period of 7 to 11 years as a criterion of success.

The results on 200 patients treated by a 3-stage 7-rib thoracoplasty are analysed. Of these 58 are discarded for various reasons. Short-term pre- and post- operative antibiotic treatment was given. Success was achieved in only 44%. Neither the acuteness of the disease, nor the size of the nodules was important, and the existence of disease in the other lung had only slight effect on the result obtained.

The size of the cavities had a different effect. Only 33% of successes were obtained when the cavities measured more than 3 cm. in diameter, against 72% when no cavity was present.

This is a valuable paper which casts doubt on the results published when less exacting bacteriological standards have been required. The authors have abandoned primary thoracoplasty in favour of resection in which they have obtained a much higher percentage of successes. *F. H. Young*

SCHAEFER, G., BIRNBAUM, S. J. & DOUGLAS, R. G. **Full-Term Delivery following Major Thoracic Surgery for Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 697–711. [15 refs.]

This rather long paper deals with 32 deliveries in 29 patients who had major thoracic surgery for pulmonary tuberculosis. 25 patients were operated on before, 3 during pregnancy, and 1 shortly after delivery.

In 25 instances no change was found; in the 5 in whom the disease was considered to be active, improvement took place, and progression of disease occurred in 2. Of the latter, treatment had been inadequate through the patient's own fault in one, and she was lost sight of; the other relapsed 5 months after delivery. The author concludes that major thoracic surgery has no more ill effects on pregnant women than those who are not pregnant. They suggest that surgery should be withheld during the last 3 months of pregnancy owing to the danger of premature delivery. A full table of details is given and the literature fully discussed. *F. H. Young*

GORDON, G. G. I. **Extrapleural Pneumolysis and Pulmonary Tuberculosis. Preliminary Hospital Results in a Series of 200 Cases.** *East African Med. J.* 1958, Sept., v. 35, No. 9, 527–32.

After a brief period of popularity in the pre-antibiotic era extrapleural pneumothorax was largely abandoned in socially advanced countries because it was used in so many unsuitable cases. In the wave of popularity of resection it has been neglected, although when used with antibiotics it is an excellent method of treatment in selected cases. Additionally the nuisance of refills makes the use of plastic space-filling material preferable to air in most cases. The author reports on the preliminary results on 200 East African patients. The details of treatment and indication used are given. The optimum length of time for continuation of refills is not discussed, although it is stated that the space was lost within 2 months in many cases. 89% of patients had sputum conversion. There was a mortality in hospital of 5·5% and 5% are still unsatisfactory. The author insisted on 3 months' pre- and 9 months' post-operative antibiotic treatment, which, in the reviewer's opinion, was the cause of his good results. He has made out a good case for the use of

this method under the special circumstances in which he has to work, especially as many patients must have been outside the categories normally accepted for this treatment. *F. H. Young*

Lu, Shih-Hsüan, Chang, Yu-Hsüan, Lin, Yu-Hua, Ho, Ch'ang-Ch'ing & Chu, Kuei-Ch'ing. **Factors affecting the Prognosis of Tuberculous Pleurisy with Effusion.** *Chinese Med. J.* Peking. 1958, Oct., v. 77, No. 4, 333–40.

The authors set out to examine the records of 50 patients who had tuberculous pleurisy in the pre- antibiotic era (group B), and 50 similar patients who were treated by the usual anti-tuberculous drugs (group A). By comparing them they hoped to answer a set of questions. Unfortunately the drug treatment was not uniform in constituent or duration.

They found that 10 cases in group A, and 12 in group B, relapsed within 2 years, but there were significantly more relapses in group B in succeeding years. In group B recurrence of tuberculosis might occur in almost any part of the body, whereas in group A it was confined to the thorax and cervical glands. The authors found that in group B relapse was more frequent where additional tuberculous lesions existed, but in group A there was little difference.

The periods during which antituberculous drugs were given were usually short, but it was clear that those who were treated for 2 months or more did better than those who had treatment for under 2 months.

F. H. Young

Chao, Yi-Ch'eng & Fang, Tu. **Tuberculoma of the Brain. A Report of Experiences on 22 cases.** *Chinese Med. J.* Peking. 1958, Oct., v. 77, No. 4, 318–26, 10 figs, on 2 pls.

This report deals with 22 consecutive cases of tuberculoma of the brain at the Tientsin Medical College. They comprised 5·3% of all intracranial tumours. 15 patients were under 20 years of age. The usual symptoms are detailed, and it is noticeable that 7 of the patients were grossly undernourished. In 15 patients the tuberculoma were situated in the cerebellum. The cerebrospinal fluid was clear in 19 of the 20 patients in which it was examined. In addition to the brain condition tuberculosis was found in lungs, bone, intestine or elsewhere in 15 patients, and in the lungs alone in 13. A tuberculoma was diagnosed or suspected in 16 of the 22 patients. Where this was done antituberculous drugs were given pre-operatively, unless the intracranial pressure symptoms were sufficiently severe to call for immediate operation; otherwise antituberculous drugs were given for varying periods post-operatively. At operation single tuberculomas were removed totally or partially in 17 patients, and multiple in 4. Of 21 patients (1 died before the brain was opened) in retrospect 3 died at, or after, operation, and 4 were not traced, 7 were able to resume work, 3 were blind, 2 had hemiplegia, 1 had severe mental deterioration, and 1 child was well after 6 months.

F. H. Young

Gernez-Rieux, C., Gervois, M. & Lebeurre, R. Protection antituberculeuse conférée à longue échéance par la vaccination B.C.G. en scarifications cutanées. L'allergie tuberculinique des anciens vaccinés. [**Long-Term Results of BCG Vaccination by Scarification**] *Ann. Inst. Pasteur de Lille.* 1957, v. 9, 57–67. [14 refs.]

This report was made to the Congress of the International Union Against Tuberculosis held in New Delhi in 1957. The work on which it is based was directed from the BCG Vaccination Centre of the Pasteur Institute in Lille where Calmette and Guérin began their now classic work on BCG early in the present century.

The study comprised 16,550 persons vaccinated by scarification in the period 1946–53 when they were aged 6–14 years. The pre-vaccinal test used was Mantoux 10 TU and only those showing induration of less than 5 mm. were vaccinated.

The vaccinated children were kept under regular medical observation along with 2 control groups of unvaccinated children of the same social environment. At the beginning none of the children were in familial contact with tuberculosis and none showed any evidence of tuberculosis at the time of inclusion in the study.

The first control group consisted of 2,352 children who were found to be non-reactors in 1948–49 and left unvaccinated; the second control group consisted of 2,036 natural reactors in the same school year of whom 327 showed induration of 5 mm., 1,447 induration of 6–12 mm. and 262 induration of over 12 mm. Both these groups were kept under medical observation also.

The persistence of tuberculin sensitivity in the vaccinated children was demonstrated by the finding that 5–9 years after vaccination the reactor rate in 2,213 was 88–100% (Mantoux 10 TU). The mean size of induration tended to increase with the passage of time. There was no evidence that the degree of sensitivity depended on the frequency of post-vaccinal testing, a finding which disagrees with that of Magnus and Edwards [this *Bulletin*, 1955, v. 30, 1060]. The authors suggest that their results may be due to the use of a highly purified tuberculin devoid of any sensitizing action. It is also mentioned that the persistently high post-vaccinal reactor rate could be due to repeated superinfection.

The natural conversion rate in the group of original non-reactors who were left unvaccinated was 61·8%, an index of the endemicity of tuberculosis in Northern France.

Tuberculosis morbidity in the various groups was compared. During the whole period of observation (4–9 years) it was 10 times higher (5/1,000 patient-years) in the unvaccinated than in the vaccinated group (0·5/1,000). It was higher in the unvaccinated non-reactors (5·67/1,000) than in the natural reactors (3·06/1,000). A high degree of tuberculin sensitivity was more often the prelude to disease than a low degree.

Primary disease was most frequent (3·91/1,000) in unvaccinated non-reactors and least frequent in original reactors (1·2/1,000). Its incidence in the vaccinated group was 0·18/1,000. Post-primary disease varied in incidence (rate per 1,000 persons annually): vaccinated,

0·12; unvaccinated non-reactors, 0·41; weak reactors 0·65; medium reactors 0·78; and strong reactors 2·44.

There was no evidence that post-vaccinal tuberculin sensitivity and acquired resistance to infection are necessarily related. Vaccination by scarification usually produces only a moderate degree of sensitivity but, as the authors' findings show, it results in a solid and durable protection. *H. G. Calwell*

LEWIS, A. G., Jr., DUNBAR, F. P., MCALISTER, Elizabeth & CACCIATORE, R. **Chronic Pulmonary Disease due to Atypical Acid-Fast Bacilli.** *Southern Med. J.* 1958, Oct., v. 51, No. 10, 1241–50, 8 figs. [19 refs.]

This article reports laboratory investigations on 80 strains of atypical acid-fast bacilli isolated from patients, and in a group of 37 of these patients clinical information is given.

3 types of bacilli have been isolated: photochromogens which were established as pathogens; non-photochromogens whose pathogenicity is still under study; and scotochromogens, usually saprophytes, but which under certain conditions may be pathogenic in abnormal lungs. In both groups approximately 6%, 75% and 13% respectively fell into the above types, 6% being unclassified.

The photochromogens tested were avirulent to guineapigs but lethal to mice. A full report of the laboratory investigation is detailed, including resistance to various drugs. Resected specimens showed pathological changes consistent with tuberculosis.

A short account is given of cases in which bacilli of each type were isolated from sputum and resected specimens. Both clinically and pathologically the cases closely resembled the lesions caused by *Mycobacterium tuberculosis*, though the response to drugs was poor.

Of the 37 patients who were fully investigated, the tuberculin test was positive in 54%, negative in 14% and not done in 32%. Clinically 61% showed marked and moderate improvement, 21% slight improvement, and 16% deteriorated after treatment. 4 patients died, 2 of bronchogenic carcinoma, 1 post-operatively, and 1 of a spread of coexisting tuberculosis. [This is an interesting and instructive paper.]

[See also this *Bulletin*, 1959, v. 34, 85.]

F. H. Young

SCHMOLLE, Stella. [Drawn by.] **Flannelgraph Cut-Outs to illustrate the Causes, Treatment, and Prevention of Tuberculosis.** 3 pp. + 12 pp. of coloured figs. 1958. London: The Sheldon Press, Holy Trinity Church, Marylebone Road, N.W.1., in association with The National Association for the Prevention of Tuberculosis. [5s.]

The Society for Promoting Christian Knowledge has joined with the National Association for the Prevention of Tuberculosis (now The Chest and Heart Association) in the production of this booklet which is intended as a visual aid to a lecture on tuberculosis to small groups in tropical areas. The booklet comprises numbered cut-out figures of a family (10 in. figure of the man), their familiar surroundings—houses or huts, cattle, domestic fowls, etc.—and a hospital. These figures, suitably backed, adhere to a blanket or other material stretched over a frame and are easily moved to illustrate the various points in the lecture.

An outline story, adaptable to urban or rural conditions, gives a straightforward account of the onset of tuberculosis in the family, the steps to be taken to obtain treatment and a simple description of the routine of such treatment. Risk of spread of the infection and the preventive measures which can be taken by the family are dealt with in careful detail.

A. H. Phipps

VENEREAL DISEASES

WILLCOX, R. R. **Venereal Syphilis and other Venereal Infections in Non-Venereal Treponematoses Areas in Africa.** *Central African J. of Med.* 1958, Oct., v. 4, No. 10, 432–43. [17 refs.]

The chief difficulties in the diagnosis and treatment of venereal diseases (VD) in Africa are due to several causes—(1) the high incidence of chancroid, (2) long foreskins which make for secondary infection, (3) confusion of non-specific spirochaetes with *Treponema pallidum*, (4) technical and biologically false positive serum reactions, (5) difficulty of follow-up and contact tracing.

Numerous figures are given concerning VD mainly in Ghana and Southern Rhodesia in 15 tables which illustrate the points mentioned above. Yaws is not considered. Gonorrhoea is the commonest form of VD, chancroid is more prevalent than in more advanced countries, dark-ground microscopy is always difficult and often impossible, serum tests for syphilis are affected by malaria, leprosy, trypanosomiasis etc., patients will rarely attend for follow-up after the disappearance of signs and symptoms, and contact tracing is seldom possible.

Until VD clinics become available most of these difficulties are insurmountable; the solution therefore lies in treating "on suspicion" all cases of genital sore, whether due to syphilis or chancroid, with 2·4 mega units of PAM (repeated in the cases of secondary syphilis); this should cure syphilis and most cases of chancroid and gonorrhoea, though sulphonamides in addition may be necessary for chancroid.

All contacts, *i.e.* all those "at risk", should also be treated in the same way.

What is stressed is that syphilis, venereally acquired, is essentially a disease of urban rather than rural areas.

T. E. Osmond

KLINE, B. S. & SUESSENGUTH, H. **Improved Emulsion of Cardiolipin, Synthetic Lecithin Antigen for the Kline Test.** *Amer. J. Clin. Path.* 1958, Nov., v. 30, No. 5, 473–6.

When cardiolipin and synthetic lecithin (CSL) emulsion was used with 1 ml. of 1% cholesterol [it is not stated what the total volume was] it was found that results were sometimes weaker than those obtained

with natural lecithin. The amount of 1% cholesterol was therefore increased to 1·25 ml. and this resulted in reactivity equal to that of natural lecithin emulsion (CNL) and greater stability.

Of 4,212 sera when 1 ml. cholesterol was used 528 were positive with CNL compared with 521 with CSL; when 1·25 ml. cholesterol was used with 5,880 sera the relative figures were 521 and 539. With 1 ml. of cholesterol the relative activities were: CSL 98·6% and CNL 100%; with 1·25 ml. of cholesterol the respective figures were 100·5% and 100%. The improved emulsion kept at 5–10°C. remains satisfactory for 7 hours and at room temperature for 1 hour.

The ingredients of the emulsion are: distilled water *p*H 6·0–6·8 containing a minimum of electrolytes, 1% cholesterol in ethanol, synthetic L-alpha-dimyristoyl lecithin solution 2½% in ethanol, cardiolipin 2½% in methanol and 0·85% NaCl. The method of preparation is set out in detail; for this the original should be consulted. *T. E. Osmond*

VINIKOFF, M. R. **The Practical Clinical Application of the *Treponema pallidum* Immobilization Test.** *Southern Med. J.* 1958, Nov., v. 51, No. 11, 1480–83. [12 refs.]

This author investigated 83 patients who gave positive serum reactions for syphilis without history or physical signs of syphilis over periods varying from 8 days to 10 years (average 3 years). The various serum tests included Kline exclusion, VDRL, Kahn quantitative and Kolmer quantitative (with beef heart or cardiolipin antigen). Tests were carried out in 2 different laboratories and there was agreement in 96%. TPI tests were carried out in all 83 cases, being positive in 55 (66·3%) and negative in 28 (33·7%). All positive reactors were placed on antisyphilitic treatment while non-reactors were not treated but advised to consult a physician because it is known that many of these suffer from other diseases, especially collagen diseases.

[It would be interesting to know what were the results of the treatment of reactors and what were the diagnoses in non-reactors. It is assumed that the TPI results were completely specific but no evidence of this is produced. There is nothing new in this article.]
T. E. Osmond

FEGELER, F. Die Bedeutung des Treponemenschwundes für die spezifische Luesdiagnostik. [**Significance of the Disappearance of Treponemata** (Treponemenschwundes) **in Specific Diagnostic Tests for Syphilis**] *Zent. f. Bakt.* I. Abt. Orig. 1957, v. 170, Nos. 1/5, 66–70. [11 refs.] Discussion 71.

Of all the tests for syphilis involving the use of a specific antigen which have been introduced in recent years, Nelson's treponema immobilization test (TPI) has proved the most trustworthy and specific. In direct comparison the *Treponema pallidum* disappearance test (TPST) [this *Bulletin*, 1956, v. 31, 710] gave 150 sera negative by TPI as 148 negative and 2 doubtful, and 214 positive by TPI as 198 positive, 3 doubtful and 13 negative.

This notwithstanding, the TPST test may be used to supplement the TPI test so as to correct some faulty results and clear up some difficult ones. If the test is to be relied on there must be disappearance of at least 80% of treponemata recognized in the control.
J. W. McLeod

DÖLLKEN, H. Zur Penicillinbehandlung der Lues in der Gravidität. [**Penicillin Treatment of Syphilis during Pregnancy**] *Deut. med. Woch.* 1958, Dec. 12, v. 83, No. 50, 2248–51.

This article contains a good discussion of penicillin treatment of syphilis in pregnancy which is based on an extensive experience. It is of the greatest importance to discover as exactly as possible the stage of the infection in the pregnant woman and to this end it should be made possible to obtain the opinion and advice of an expert in venereal disease in all cases. The author also deplores the practice, which is frequent, of giving all pregnant women who have had syphilis a "safety treatment" with penicillin even when they have been adequately treated and supervised for a satisfactory period before conception.

The treatment of the mother and of the child which is advocated in different circumstances or stages of the infection as revealed by serological and clinical investigations is described. Most of the cases in which expert advice is sought are in women who have already been treated for syphilis. These cases may present considerable difficulty and require great practical experience for their evaluation; they may be classified as those in which (1) treatment was adequate in accord with accepted standards and followed by a 2-year period of sero-negative follow-up, (2) treatment was adequate but the subsequent period of supervision was too short, (3) treatment was considered to have been inadequate in spite of negative serum tests, and (4) treatment was considered to be adequate but the serum reactions continued to be more or less strongly positive.
M. E. Delafield

WILLCOX, R. R. **The Aetiology of Non-Gonococcal Urethritis.** *Brit. J. Clin. Practice.* 1958, Dec., v. 12, No. 12, 883–7. [Numerous refs.]

Non-gonococcal uretheritis (NGU) first became prominent during World War II and has increased steadily during recent years, the figures for England and Wales rising from 10,794 in 1951 to 14,829 in 1956. It is thought to be acquired mainly during sexual intercourse but the causative organism is not known; the 5 possible causes are (1) bacteria, (2) trichomonads, (3) spirochaetes, (4) pleuro-pneumonia-like organisms (PPLO) and (5) viruses.

The most common bacterium found is *Staphylococcus albus* with diphtheroids a poor second but it does not seem likely that either is the causative organism; a proportion of cases of NGU show trichomonads but many do not; spirochaetes have been demonstrated in the discharge and are thought to be similar to those found in the mouth but appear to account for only 1·9% of cases; PPLO have been found frequently in NGU but also in controls and are probably merely commensals; viruses are thought by most people to be the most likely cause but though skin tests were positive

in a high percentage of cases serum tests, Giemsa-stained urethral scrapings and animal experiments gave little positive evidence.

The conclusion therefore is that the cause of NGU is still not yet known. *T. E. Osmond*

VERHEYE, H. & KANDA, D. Les uréthrites à trichomonas. **[Trichomonas Urethritis]** *Ann. Soc. Belge de Méd. Trop.* 1958, Apr. 30, v. 38, No. 2, 231–5.

Struck by the large number of patients with a urethral discharge in which gonococci could not be found, these authors searched for *Trichomonas vaginalis* (TV) in Africans in the Belgian Congo. In general, patients did not complain of pain or any urinary symptoms but showed a urethral discharge which was opaline or frankly purulent with few or many pus cells.

To find TV they examined a drop of urethral discharge or of centrifuged urine on a slide under the microscope; they never isolated the organism from the preputial fold.

In 912 patients, taken at random, there was a mucoid discharge in 139, a purulent discharge in 70 and no abnormal secretion in 703. TV was found in 70 of the first group, in 37 of the second and in 21 of the third.

An examination of 432 women showed that 33% of those married and 32% of those single were infected. 37% of wives of infected husbands were positive and 47% of husbands of infected wives were positive. 54 patients were treated with a solution consisting of gentian violet 2 gm. lactic acid 2 gm. and water to 100 ml.; the treatment involved irrigation of the urethra twice daily for 7 days. Examination 2 days and again 9 days after completion of treatment showed that all except 1 were cured.

[Treatment seems to have been much more successful than that applied in Great Britain; one wonders whether it was equally successful in the female.]

T. E. Osmond

WANG, T'ung-Kuan & HSIA, Tsung-Fu. **Treatment of *Trichomonas vaginalis* Infections with Plant Germicides and Medicinal Herbs.** *Chinese Med. J. Peking.* 1958, Oct., v. 77, No. 4, 363–8.

In order to test the efficacy of certain plant germicides 1,460 women from a cotton mill at Nantung, China, were examined for *Trichomonas vaginalis* (TV); 394 (26·9%) were positive by hanging drop and 448 (30·6%) were positive by culture; total positives were 457 (31·3%). The incidence was considerably higher in those who used common wash basins, towels etc., than in those who used individual ones, *i.e.* 29% as against 17%. Signs and symptoms varied from little discomfort to abundant discharge. Specimens from cervical secretion were positive in 35·83%, from urethral secretion in 4·28% and from the urine in less than 1%, of 187 cases.

The plant germicides employed were onion, ginger and turnip; the vegetables were peeled, washed with water, immersed in potassium permanganate, washed again, cut in pieces and crushed; turnip juice was used undiluted, onion was diluted 1/2 and ginger diluted 1/4. Treatment consisted in swabbing the vagina, after flushing with warm water, with the juice and then leaving a tampon impregnated with the juice *in situ* for 8–10 hours. This treatment was repeated daily for 10 days.

Cure rates were:—23·4% with onion, 35·9% with turnip and 17·6% with ginger; somewhat better results were obtained when treatment was continued for 15 days, cure rates being 38·7, 46·9 and 31·4% respectively. However, relapse rates were high, being 75·0, 63·1 and 78·5% respectively. When the vagina was flushed with 1% acetic acid before the application of turnip juice the cure rate after 15 treatments was 100% in previously untreated cases and 82% in those previously treated with turnip juice; it is thought that the action of the 2 remedies was synergic.

Other substances employed were *Gleditshia glauca* and *Lychnis* sp. which gave cure rates of about 65% and relapse rates of about 20%; with these substances the vagina was first flushed with 0·5% lactic acid. Infection of the bladder was well controlled by 4% boric acid solution.

[The remedies named above do not seem to have been more effective than those commonly used in Western countries; most remedies are effective temporarily but relapse is almost inevitable.]

T. E. Osmond

OTHER COMMUNICABLE DISEASES

The order of papers in this section is as follows: Tetanus; other diseases

PROC. ROY. SOC. MED. 1958, Dec., v. 51, No. 12, 997–1008 (Sect. Exper. Med. Therap. with Sect. Neurol), 2 figs. [29 refs.] **Discussion on Tetanus** [WRIGHT, G. P.; LAURENCE, D. R.; ADAMS, E. B.; SMITH, A. C.]

Dr. G. Payling WRIGHT discusses the fate of tetanus antitoxin after injection into the human body. After a dose of 100,000 units the antitoxin titre in the serum is still 15 units per ml. after 9 days, falls to 1 unit in 4 weeks and to 0·1 unit after 7 weeks. After a dose of 1,500 units, the usual prophylactic dose in Britain, the titre falls to 0·2 unit in 2 weeks and to 0·01 unit in 3 weeks. The protective titre is probably between 0·1 and 0·01 unit. Repeated injections may not be successful in maintaining a high titre for the body becomes immunized against the foreign protein and may destroy it so quickly after repeated injections that the injected antibody has no protective effect at all. He illustrates this by quoting the case of a boy who after an injury to his hand did not develop tetanus after an injection of 1,500 units tetanus antitoxin but who, after an identical injury 6 months later developed tetanus and died in spite of 1,500 units antitoxin given prophylactively and 100,000 units given intravenously in treatment. The author recommends that once a patient has been given any horse serum antitoxin he should

be immunized actively against diphtheria and tetanus with the appropriate toxoid. He also recommends active immunization against tetanus before operation on tissues which have been traumatized and may be harbouring tetanus spores.

Dr. D. R. LAURENCE discusses experiments designed to test the antitetanic action of drugs in rabbits. The phenothiazines (chlorpromazine, acetylpromazine and promethazine) were the most potent of those tried which included barbiturates, mephenesin, benzimidazole derivates and beta-naphthoxyethanol. It appeared that giving chlorpromazine more frequently than every 2 hours might result in the disappearance of antitetanic activity in the rabbit, and increasing the dose above 3–5 mgm. per kgm. body weight might not increase antitetanic activity. It is, however, essential in the human being to give adequate dosage and the author refers to 2 articles published in the same issue of a journal in 1958: in one chlorpromazine given in modest dosage "seemed to have no specific effect", [this *Bulletin*, 1958, v. 33, 339] in the other "large doses controlled the convulsions" [*ibid*, 340]. The author stresses the difficulty but importance of assessing clinically the antitetanic properties of drugs.

Professor E. B. ADAMS describes clinical trials on 171 Indian or African patients treated for tetanus, 71 being neonates. Chlorpromazine and phenobarbitone were compared in one trial, and chlorpromazine alone and mixtures of chlorpromazine and phenobarbitone or chloral hydrate in a second trial. Critical assessment of the results did not show statistical differences between the groups. Period of onset was of greater prognostic significance than incubation period, though this too was important. The author was unable to classify the causes of death in tetanus; often autopsy did not reveal an adequate cause though varying respiratory complications were seen. Exhaustion from spasms might be important in neonates, but should not be in older patients in whom spasms were more easily controlled. Over-sedation was a danger especially in neonates and tetanus intoxication of the medullary centres might be the most important cause of death from tetanus. Critical evaluation of antitetanic drugs was essential, results based on small series of cases often being misleading.

Dr. A. Crampton SMITH reported the treatment of 7 patients by curarization, tracheotomy and intermittent positive pressure ventilation: 4 of the patients survived. He believed this to be the only possibility of survival in the most severe cases of tetanus.

A. B. Christie

CHARLAS, R., HAJJAOUI, Y. & XARDEL, H. A propos de 25 cas de tétanos ombilical observés dans le service de pédiatrie de l'Hôpital Mohammed V durant l'année 1957–1958. **[25 Cases of Umbilical Tetanus Seen in the Children's Department of the Mohammed V Hospital in Morocco in 1957–1958]** *Maroc Méd.* 1958, Oct., v. 37, No. 401, 1022–6, 1 map.

Of 25 babies in the first month of life suffering from umbilical tetanus only 2 survived. Treatment was by antitetanic serum, penicillin and streptomycin and sedation with chlorpromazine, phenobarbitone and promezathine: muscle relaxants were used in 10 cases without obvious effect but curare was not used, nor tracheotomy performed. Nearly all the patients were seen at a late stage and hospital facilities were not ideal. The cause of the tetanus was only too obvious in the conditions of childbirth, delivery frequently taking place on the earthen floor and grossly contaminated instruments being used. Cases occurred mainly on the outskirts of the town where houses have earthen floors and animals live in the adjoining yards: where houses had paved or mosaic floors cases of tetanus were rare. The authors feel that the main treatment must be prophylactic and educational. *A. B. Christie*

KOURANY, G., CLEVE, E. A. & SMITH, F. P. **Treatment of Tetanus. Therapy of Tetanus from 1905 to 1956, Gorgas Hospital.** *Arch. Intern. Med.* 1958, Nov., v. 102, Nov. 5, 823–9.

This is a review, but not a very detailed one, of 70 cases of tetanus occurring from 1905 to 1956 at Gorgas Hospital. The authors discuss the treatment of tetanus with regard to the management of the wound or source of toxin, the neutralization of circulating antitoxin and the suppression of symptoms due to toxin fixed in the central nervous system. They conclude that antitoxin is the proper treatment for circulating toxin, and that sedation, with prophylactic tracheotomy, should control the convulsive stage. They believe that local treatment of the wound has little effect on the outcome in a case of tetanus but reached this conclusion only after they had performed hysterectomy in 3 young women suffering from tetanus.

A. B. Christie

PODVARKO, A. G. **The Treatment of Tetanus.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 11/12, 1798–1802. [Translated from Russian.]

This is a review of 35 patients suffering from tetanus treated at the Dagestan Medical Institute from 1939–54: 6 patients died. Sedation was secured mainly by chloral hydrate given rectally in doses of 2 gm. once or twice a day. Tetanus antitoxin was given daily for approximately 7 days though the authors state that it is best to give the largest possible amount in 1 dose. Tetanus toxoid was also given, the first dose along with the antitoxin, the second 10–12 days later. Penicillin was also given and omnopon, morphine, phenobarbitone and bromural were used to supplement the chloral hydrate. The patients were given a hot bath every morning: they became relaxed and were given most of their food while in the bath.

A. B. Christie

IKIC, D. **Amount of A.U. in Subjects vaccinated with P.T.A.P. Tetanus Prophylactic.** *Acta Med. Iugoslavica.* 1958, v. 12, Nos. 1/2, 179–85.

The antigenic potency of a preparation of tetanus toxoid treated with aluminium phosphate and containing 10 Lf per ml. was compared with that of the same

amount of toxoid mixed with 10^9 heat-killed *Salmonella typhi* and $2{\cdot}5 \times 10^8$ heat-killed *Salmonella paratyphi B*. Each preparation was used to immunize a group of young adult men, in a dosage of 3 injections of 1 ml. at intervals of 30 days.

The minimum level of serum antitoxin considered to afford protection against tetanus is 0·01 units per ml. This level was achieved 30 days after the first injection in 69 of 71 men who were given combined prophylactic and in 57 of 70 who received pure toxoid. 30 days after the second injection all of 43 immunized with the combined preparation and all but 1 of 77 given pure toxoid had a serum level of 0·01 unit per ml.

A week after the third dose all those given combined prophylactic had more than 1 unit per ml. in their serum, and of 64 given pure toxoid 13 had between 0·1 and 1 unit and the remainder had over 1 unit.

These findings show that the addition of killed typhoid and paratyphoid bacilli to tetanus toxoid treated with aluminium phosphate exerts an adjuvant effect as it is also known to do with pure formol toxoid.

I. B. R. Duncan

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order:—General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; others.

For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

GARGANI, G. & GUERRA, M. La brucellosi umana in Italia negli anni 1946–57. Rilievi statistici ed epidemiologici. [**Human Brucellosis in Italy in 1946–57. Statistical and Epidemiological Observations**] *Ann. d. San. Pubblica.* Rome. 1958, July–Aug., No. 4, 747–89, 7 figs. [34 refs.] English summary.

Human brucellosis in Italy appears linked with sheep rearing, bovine foci also arising secondarily from association with sheep. *Brucella melitensis* is practically the only species concerned.

Submitting the monthly figures for human infections to a process of periodal analysis, the authors conclude that the chances of contracting brucellosis increase from November to May and then decrease at a slower rate. Incidence agrees with the periods of ovine reproduction and the relation, all things considered, appears to be a causal one. After a very detailed mathematical analysis it is concluded that there is also a group of factors which produce their effects in late summer and autumn, the number of cases due to them being much smaller, differing from the fundamental causes which act in the spring.

The authors attempt to study the correlation between the size of the animal population and the degree of endemicity of brucellosis: a positive relation is found to exist with infection in sheep, but this conclusion could only be very tentative considering the difficulty of collecting accurate data. (Among other points the authors could only consider the total animal population without considering the proportion of animals which are infected.)

141 strains were examined between 1952 and 1958, of which 9 were typical *melitensis*, 128 atypical *melitensis*, (with *melitensis* characters but *abortus* serology, corresponding to Renoux's "intermediate" type), 1 typical and 2 atypical *abortus* and 1 *suis*. [This number of strains is extremely small for a 7-year period.] The atypical *melitensis* is said to be characteristic of Mediterranean countries, pointing again to the sheep as the main infecting agent.

A human endemicity index varies from 9·81 per 10,000 in the province of Enna, in Sicily, to one of 0·07 in Bolzano. One gets the impression that brucellosis is on the increase especially in places where it had been scanty or absent and that it is stationary or decreasing in areas where it has been endemic. Besides pasteurization of milk and other general measures, prophylactic vaccination of sheep and goats is considered as the measure most likely to reduce incidence.

E. Agius

MCKEEVER, S., SCHUBERT, J. H., MOODY, M. D., GORMAN, G. W. & CHAPMAN, J. F. **Natural Occurrence of Tularemia in Marsupials, Carnivores, Logomorphs, and Large Rodents in South-Western Georgia and Northwestern Florida.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 120–26, 2 figs. [13 refs.]

A search for infection with *Brucella tularensis* on 2,004 wild mammals representing 13 species showed that 17·2% had agglutinins at titres of 1/80 or over. More than 20% of racoons, grey foxes, striped skunks and wildcats, and over 10% of spotted skunks, opossums and red foxes, had significant titres. The rate of infection appeared to vary directly with the density of the vegetation especially in areas having many swamps and bottomland hardwood forests, which latter favour arthropod vectors. Spleens from 80 reacting animals were cultured, *Br. tularensis* of a highly virulent character being isolated from one only, coming from an opossum with an agglutinating titre of 1/1,280. It is concluded that mammals other than rabbits (which are usually inculpated), can infect man who hunts them for food, sport or fur, directly or through blood-sucking arthropods or contaminated water.

E. Agius

KARTMAN, L., MURRAY, K. F., PRINCE, F. M., QUAN, S. F. & HOLMES, M. A. **Public Health Implications of the *Microtus* Outbreak in Oregon and California during 1957–1958.** *California Vector Views.* 1958, Apr., v. 5, No. 4, 19–24.

During 1957–8 an unusually high population of meadow voles (*Microtus*) was observed in parts of Oregon and California, the largest and most extensive yet recorded in North America. Surveys of the outbreak were made and this report presents data on diseases transmissible to man from the vole population.

Animals captured alive and kept isolated for 25 days showed a death rate of 27% from tularaemia but about 40% of the deaths in that time were not due to any identified rodent disease. Tularaemia was found also in a high percentage of dead voles from various areas, suggesting the presence of an active epizootic. Practically no fleas, but numerous mites and lice, were found on either dead or live voles or in their nests. The fleas, mites and lice were inoculated into laboratory animals and white mice developed tularaemia after inoculation from 1 pool of 10 mites. *Pasteurella pestis* was isolated from 2 of the voles in Oregon. The mode of transmission is difficult to determine as practically no fleas were found.

Tests showed that *Microtus* is highly susceptible to tularaemia. The mode of transmission in nature is probably cannibalism in delimited areas of high population density.

Further significant tularaemia findings implicated water from streams, irrigation channels and a shallow well. Of 30 water samples from Oregon counties and 1 from N. California 7 (23%) yielded the organism of tularaemia.

The presence of tularaemia epizootics in *Microtus* and its contamination of water poses a very definite public health problem. *P. A. Clearkin*

PARNAS, J. Studien über die Diagnostik einiger professionellen Erkrankungen auf dem Lande: Forschungen über die immunobiologischen Para-Reaktionen bei Brucellose und Tularämie. [**Skin Reactions in Brucellosis and Tularaemia**] *Arch. f. Hyg. u. Bakt.* 1958, Oct., v. 142, No. 7, 494–505.

Investigating sera from cases of disease and from experimental animals, the author has confirmed the finding reported by others that crossed reactions of agglutination in brucella and tularaemia infections are common.

He has found the same to hold for complement fixation reactions and for observations on phagocytosis depending on increased content of the serum in opsonin.

The allergic skin reactions to brucellin and tularin respectively do, however, furnish a reliable means of differentiating between these two diseases.

J. W. McLeod

CHUNG, Huei-Lan, CH'IU, Fu-Hsi, WU, Hsüeh-Tsung, HOU, Tsung-Ch'ang & K'UANG, Ch'i-Hung. **Leptospirosis. A Clinical and Statistical Study of 182 Cases.** *Chinese Med. J.* Peking. 1958, Sept., v. 77, No. 3, 207–35. [27 refs.]

CONSTANTINESCO, N. & ZAVATE, Olga. Recherches immunologiques dans les leptospiroses. [**Immunological Studies on Leptospirosis**] *Ann. Inst. Pasteur.* 1958, July, v. 95, No. 1, 41–8. [12 refs.]

In order to study certain problems of immunity in leptospirosis, white rats were inoculated with strains of *Leptospira canicola, L. grippotyphosa, L. pomona* and *L. sejroe.* After a preliminary leptospiraemia lasting about 4 days the micro-organisms established themselves in the kidneys where they were found to persist for at least 200 days. Antibodies could be detected by means of Pfeiffer's reaction and agglutination tests as early as 3 days after inoculation. The agglutination reaction was strictly specific; co-agglutinins for heterologous serotypes, which are common in infections of other animals including man, were never found in the rat sera.

Good antibody responses were also obtained by inoculating the rats with a formolized vaccine of *L. pomona,* and vaccination of workers in pig-breeding establishments is recommended since surveys showed high rates of infection among the pigs and the men in contact with them.

Other experiments were concerned with the transmission of passive immunity from dams to their offspring. To discriminate between antibodies transmitted *via* the placenta and those acquired by suckling, the young of infected dams were nursed by normal rats whose own offspring were suckled by the infected dams. Antibodies were present at birth in the sera of the young of infected dams, but had disappeared by the twentieth day when suckled by normal rats. Antibodies became demonstrable in the serum of normal young rats at about the tenth day of nursing by infected dams. It appeared therefore that antibodies were transmitted through the placenta and also by suckling.

J. C. Broom

COMBIESCU, D., STURDZA, Nina, SEFER, M. & RADU, I. Leptospirenforschungen in Rumänien. [**Research Work on Leptospira in Roumania**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 103–6.

A summary of work carried out to determine the incidence of leptospirosis in Rumania was published by Combiescu *et al.* [this *Bulletin,* 1957, v. 32, 1151], and the present article contains further information on the subject. In addition to the serotypes of leptospires previously known in Rumania, *Leptospira bataviae* and *L. sejroe* have now been isolated in culture, and serological evidence has been obtained which suggests that *L. autumnalis* and *L. hebdomadis* are present also.

Large variations in the incidence of human leptospirosis were noted from year to year: 990 cases occurred in 1955 as compared with 242 in 1956 and 76 in 1957. Up to 1956 *L. pomona* infections constituted 65% of the total but in 1957 the figure fell to 20%. Unfortunately there was no opportunity of determining whether there was a concurrent fall in infection rates among pigs.

The curious observation was made that more than 15% [from a statement elsewhere in the text this may be a misprint for 50%] of sera from human cases agglutinated the Patoc strain of *L. biflexa* which has certain antigenic components related to those of *L. autumnalis* and *L. semarang.* The reactions were most marked with sera from *L. pomona* infections (67%) and *L. canicola* (55%). The authors suggest that the effect is probably of the nature of the "paradoxical reaction" first described by FÜHNER [*ibid.,* 1951, v. 26 607] but they point out that COX [*ibid.,* 1958, v. 33, 343] obtained an extract from strains of *L. biflexa* which acted as a genus-specific antigen in the erythrocyte sensitization test.

500 small rodents, including *Apodemus flavicollis, A. sylvaticus, Microtus arvalis* and *Mus spicilegus*, were examined but none showed evidence of infection with leptospires. 6 land tortoises (*Testudo graeca*) were also negative, but the sera of 10 out of 11 pond tortoises (*Emys orbicularis*) had high antibody titres for *L. hyos* though no leptospires could be demonstrated in their kidneys. This contrasts with the high infection rates found among domestic animals [Combiescu *et al., loc. cit.*] which presumably provide the source of human infections. *J. C. Broom*

Cox, C. D., Stover, R. C. & Treick, R. W. **Serological Studies on Hemolytic Antigen from Leptospira.** *Proc. Soc. Exper. Biol. & Med.* 1958, June, v. 98, No. 2, 265–9. [11 refs.]

A genus-specific antigen which could be used for the serological diagnosis of leptospirosis was isolated from a strain of *Leptospira biflexa* by Cox and his colleagues [this *Bulletin*, 1958, v. 33, 343]. Further studies are reported here on this "HL antigen", which is considered to be a polysaccharide probably combined with some nitrogenous material of low molecular weight.

Rabbits inoculated with suspensions of whole cells of *L. biflexa* produced both type-specific agglutinins and HL antibodies whereas cells repeatedly extracted with 50% ethanol elicited only agglutinins. The antibodies produced by inoculation of HL antigen, either alone or adsorbed on to rabbit erythrocytes, were predominantly of HL type though the antisera had also low agglutinin titres—possibly because the HL antigen had not been completely purified. By appropriate absorptions, antisera were prepared containing only agglutinins and only HL antibody respectively and these sera were used to study the precipitating and complement-fixation properties of the 2 types of antibody.

In precipitin tests, antisera containing only HL antibody gave no precipitation with HL antigen. Antisera containing only agglutinins precipitated with HL antigen, but only in very low dilutions and presumably due to the presence of traces of agglutinogens in the antigen as mentioned above. Similarly in complement-fixation tests serum containing HL antibody failed to fix complement in the presence of complete cells, ethanol-extracted cells or HL antigen, whereas agglutinating sera fixed with all three.

It appears therefore that HL antibody plays no part in leptospiral agglutination, precipitin or complement-fixation reactions. *J. C. Broom*

Diseases due to Fungi

For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

Drouhet, E. Revue critique de la mycologie medicale entre 1946 et 1956 en France et dans l'Union Française. [**Critical Review of Medical Mycology during 1946–1956 in France and the French Union**] *Mycopathologia.* The Hague. 1958, Nov. 20, v. 10, No. 1, 19–40, 1 fig. on pl. [172 refs.]

The main sections of this review are on ringworm and dermatophytes (pp. 19–21, 21 refs.) and moniliasis and *Candida* (pp. 21–25, 48 refs.); aspergillosis (pp. 25–26), cryptococcosis, histoplasmosis, sporotrichosis, chromoblastomycosis, mycetoma, actinomycosis and miscellaneous mycotic conditions being treated more briefly. *G. C. Ainsworth*

Richter, R. & Erbakan, N. Der heutige Stand der medizinischen Mykologie in der Türkei. [**Present Position of Medical Mycology in Turkey**] *Mycopathologia.* The Hague. 1958, Nov. 20, v. 10, No. 1, 41–52, 2 figs. [38 refs.]

This review of mycoses encountered in Turkey is based on clinical and mycological studies of 3,007 patients at the mycological laboratory of the *Klinik und Poliklinik für Haut- und Geschlechtskrankheiten*, Ankara University, from its establishment in June 1953 to the end of 1957.

Trichophyton violaceum is the principal agent of tinea capitis, corporis and barbae. *T. schoenleinii* was the sole agent of favus. *Epidermophyton floccosum* and *T. interdigitale* were the prevalent agents of onchomycosis. Pityriasis versicolor [*Malassezia furfur*] is fairly frequently met with.

Among the deep-seated mycoses, cases of *Candida albicans* and *Cryptococcus neoformans* infections were seen, and there were occasional cases of histoplasmosis (*Histoplasma capsulatum*), sporotrichosis (*Sporotrichum schenckii*), rhinosporidiosis (*Rhinosporidium seeberi*), Madura foot [agent unidentified], actinomycosis [agent unidentified], and aspergillosis (*Aspergillus fumigatus*). *G. C. Ainsworth*

Williams, D. I., Marten, R. H. & Sarkany, I. **Oral Treatment of Ringworm with Griseofulvin.** *Lancet.* 1958, Dec. 6, 1212–13.

Griseofulvin was first isolated as long ago as 1939, as a metabolic product of *Penicillium griseofulvum*

dierckx, an antibiotic with antifungal properties (OXFORD, RAISTRICK & SIMONART, *Biochem. J.*, 1939, v. 33, 240).

The toxicity of griseofulvin administered by mouth to mammals is very low and it is notable that single oral doses do not kill mice at a level of 50 gm. per kgm. body weight or rats at a level of 10 gm. per kgm.

9 patients with clinical *Trichophyton rubrum* infection of the skin or nails were treated, the arbitrary dose being 0·5 gm. 4 times a day. No local treatment was used. Patients reported rapid relief of itching when it had existed previously, and in 3 cases the reappearance of sweating previously absent for many years. Infected nails appeared to be growing out with regular increases in the extent of normal nail below the clinically infected area. The skin of the palms lost its hyperkeratosis and approached the normal appearance in 2 or 3 weeks, while the fungus became increasingly difficult to find in scrapings.

One case of *Microsporon audouinii* infection of the scalp was treated and after 3 weeks the fluorescence under Wood's light became dull and lustreless, and hair with no fluorescence and no fungus was seen growing out from the scalp. No side effects of any importance were observed in these patients.

The authors consider that griseofulvin may be of therapeutic value although its uses and limitations are not yet well established and the optimum dosage and duration of treatment must yet be discovered.

H. T. H. Wilson

FOX, E. C. & AINSWORTH, G. C. **A Contribution to the Mycology of the Mouth.** *Brit. Med. J.* 1958, Oct. 4, 826–8. [10 refs.]

An examination was made at the Birmingham Dental Hospital during 1952 to 1955 of 149 patients grouped into 6 clinical categories; angular cheilosis (24), gingivostomatitis (36), lingua nigra (40), lingua geographica (22), coated tongue (20) and denture sore (7), and a group of 188 controls consisting of school children, university students, professional and office workers.

It was concluded that *Candida albicans* probably played a significant part in the aetiology of angular cheilosis and possibly also in that of gingivostomatitis, this species being isolated from 70·8% of the former group and 52·8% of the latter. With regard to the other 4 clinical categories the mycological picture was so varied that it supported the view that these conditions are not of fungal origin. *Candida albicans* was also isolated from 27·7% of the control group.

Little evidence was found of a characteristic fungal flora of the mouth; a total of 76 different species was isolated from the combined normal and abnormal groups.

Jacqueline Walker

RÖTTER, W. & STAIB, F. *Candida tropicalis*-Pneumonie. Behandlung und Verlauf. [**Pneumonia due to *Candida tropicalis*: a Case Report**] *Deut. med. Woch.* 1958, Dec. 19, v. 83, No. 51, 2285–8, 2299, 2315, 6 figs. on pl. [30 refs.]

In this paper the authors make reference to the literature on mycosis of the lungs and other organs and point out that the disease must occur more frequently than it is diagnosed. The diagnosis of candidiasis of the lungs is shortly considered and there is a description of the morphological characters and biochemical reactions of *Candida tropicalis* which was found to be the cause of the pneumonia in the case described here.

The patient was a man 56 years of age with no important past history who was taken ill with a temperature reaching 40°C. at night, rigors, pains in the chest and cough. The daily amount of sputum was estimated to be 200–300 ml. A diagnosis of pneumonia was made by the medical practitioner who prescribed penicillin treatment. After 10 days the patient had not improved and he was admitted to hospital. His clinical condition and the signs on auscultation are described. X-ray of the lungs revealed extensive infiltration on both sides. The sputum was copious and was found to contain leucocytes and yeasts. Treatment by achromycin [tetracycline] and sulphonamides was instituted and the patient became afebrile after a few days but then the temperature rose afresh. In the meantime *Candida tropicalis* had been isolated in profusion from the sputum and thereupon treatment with trichomycin was begun. This antibiotic was given in dragées, at first 3 (50,000 units each) per day and later 5 or 6 per day. In a week the temperature had fallen to normal. Treatment was continued for 3 weeks (100 dragées *i.e.* 5 million units in all had been given) and the X-ray picture was then greatly improved and *Candida tropicalis* was not found in the sputum. The patient made an uninterrupted recovery. There are photographs of the X-ray appearances on admission, after 14 days of treatment and 4 weeks after discharge.

Trichomycin, obtained from *Streptomyces hachijoensis*, was first described in 1952 by HOSAYA, who found it to be active against a number of yeasts and moulds. Reports on its therapeutic value in mycoses of the lungs have been made by several workers.

In the discussion a warning is given that the satisfactory outcome of this case does not warrant the opinion that the problem of the treatment of mycosis has been solved.

(Trichomycin is marketed by the Fujisawa Pharmaceutical Co., Osaka, Japan.)

M. E. Delafield

GIUNCHI, G. **Candidosis following Antibiotic Therapy.** *Scientia Med. Italica.* 1958, v. 6, No. 4, 580–628. [Numerous refs.]

In this lengthy paper the author reviews the present knowledge of the various forms of candidiasis which may result from antibiotic therapy and incorporates some of his personal observations on the subject. The article is completed by a valuable bibliography consisting of some 130 references.

Jacqueline Walker

HOSTY, T. S., AJELLO, L., WALLACE, G. D., HOWELL, J. & MOORE, Jane. **A Small Outbreak of Histoplasmosis.** *Amer. Rev. Tuberculosis.* 1958, Oct., v. 78, No. 4, 576–82, 1 fig. [12 refs.]

During the last 20 years many outbreaks of histoplasmosis have been reported in the United States and

a large number of them have been associated with the clearing of neglected chicken houses. [LEHAN, P. H. & FURCOLOW, M. L., *J. Chronic Dis.*, 1957, v. 5, 489. See also this *Bulletin*, 1958, v. 33, 346, *bis*.]

In the present outbreak which occurred in Dallas County, Alabama, a known endemic area, a father aged 36, his son and daughter aged 5 and 3 years respectively, developed histoplasmosis 15 to 19 days after spreading manure of uncertain origin, but believed to have been collected near an old chicken house. The symptoms of all 3 were those of an atypical pneumonia, and X-ray examinations showed pulmonary densities. However, it was not until the father's infection proved fatal and a necropsy was performed that the correct diagnosis was established histologically and by culture. No mycological examination was made in the case of the children, their infections being confirmed serologically.

2 soil samples which were taken from the fertilized flower beds each yielded *Histoplasma capsulatum*.

Jacqueline Walker

DAOUD, K. A. & SCHWABE, C. W. **A Skin-Test Survey for Histoplasmosis and Coccidioidomycosis in the Middle East.** *Amer. J. Trop. Med. & Hyg.* 1958, Nov., v. 7, No. 6, 643.

"None of a total of 2,030 Middle Eastern nationals tested was positive to histoplasmin or coccidioidin."

STAPFF, V. H. & MACKINNON, J. E. Tratamiento de un caso de histoplasmosis con diamidinodifenilamina. [**A Case of Histoplasmosis treated with Diamidinodiphenilamine**] *An. Facul. de Med. Montevideo.* 1958, May–June–July–Aug., v. 43, Nos. 3/4, 116–21. [26 refs.]

The English summary appended to the paper is as follows:—

"A chronic case of histoplasmosis and tuberculosis in an adult male has been studied. *Histoplasma capsulatum* was observed and cultivated from the oropharyngeal ulcerous lesions and it is presumed that the fungus was the only cause of these lesions. Pulmonary lesions, probably of a mixed nature, were present. After a short treatment with isoniacid and streptomycin an aromatic diamidine, diamidinodiphenylamine dihydrochloride (M. & B. 938) was administered intravenously in daily doses of 150 to 250 mgs. Two series of 11 and 10 injections separated by a rest period of 22 days were given. The total dose was 4.6 gs. After ten days of treatment the favourable effect of the drug over the oropharyngeal ulcerations was evident. At the end of the treatment and after the ablation of the remains of some carious teeth healing was completed. No relapses were observed 8 months after the end of the treatment. The pulmonary lesions improved very little."

RAZIN, S., COHEN, Ada & ROZANSKY, R. **Antimycotic Effect of Spermine.** *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 459–62, 1 fig.

"1) Spermine inhibited growth of several species of yeasts, *Saccharomyces* and *Debaryomyces* species being the most sensitive. The antimycotic effect of spermine was more pronounced at an alkaline pH and was antagonized by inorganic salts. The adsorption of spermine by yeast cells was significantly smaller than by *Staph. aureus*. 2) Spermine retarded the death rate of washed cells of *S. cerevisiae* suspended in tris buffer. A pronounced killing effect of spermine was observed when glucose was added to the buffer."

Rheumatic Diseases

CONYBEARE, E. T. **Notified Acute Rheumatism 1950-57.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, Nov., v. 17, 244–9.

Since 1950 acute rheumatism in a child under 16 years of age has been notified in 6 urban and 2 predominantly rural areas of England and Wales, with, together, a population of approximately half a million children (the County Boroughs of Bristol, Grimsby, Kingston-upon-Hull, Lincoln, Salford and Sheffield and the administrative counties of Cornwall and Lincolnshire, Parts of Lindsey). Between January 1950 and December 1957, 981 new cases were notified of whom one-half had active rheumatic heart disease. Rates in relation to the estimated numbers of children at risk show a higher incidence in girls than in boys (2·50 per 10,000 to 2·05) and an increase in incidence with rising age to a peak at 10–15 years (3·90 in boys and 4·67 in girls per 10,000). The annual incidence showed little change between 1950 and 1954 but declined considerably in 1955 and remained low (about 2·5 per 10,000 in the earlier period compared with only 1·5 per 10,000 in the final years). The rate was relatively high in the County Boroughs of Salford and Sheffield (3 to 4 per 10,000) and low in Kingston-upon-Hull, Lincoln and the Lincolnshire Parts of Lindsey (1–1½ per 10,000). Notifications of rheumatic chorea in boys were 2·0 per 100,000 (about one-tenth the total of acute rheumatism). In girls the incidence was more than twice as high—4·9 per 100,000 (about one-fifth the total of acute rheumatism). In the 10–15 year age group chorea was 3 times as great in the girls as in the boys.

A. Bradford Hill

HOLLISTER, L. E. & ENGLEMAN, E. P. **Rheumatic Fever in Military Personnel.** *U.S. Armed Forces Med. J.* 1958, Oct., v. 9, No. 10, 1436–43. [10 refs.]

This review of 563 cases of rheumatic fever occurring in U.S. military personnel during World War II is not

remarkable for anything new. There was a previous history of rheumatic fever in about one-third of the patients, and a closely antecedent history of an acute upper respiratory tract infection in 85%, of which evident streptococcal infection amounted to 66%.

The most important clinical manifestation was acute polyarthritis (85%). It was self-limiting and responded rapidly to salicylate therapy. Carditis was diagnosed in 41%, a systolic murmur usually being present, and commonly also electrocardiographic signs, especially A-V block and ST-T wave abnormalities. Fever, arthralgia and elevated ESR were common, but erythema marginatum, subcutaneous nodules and chorea were rare in these young adult patients. Residual heart disease was diagnosed in 20%. *H. Stanley Banks*

Scheff, G. J., Marienfeld, C. J. & Hackett, Eloise. **Blood Culture Studies in Rheumatic Fever Patients.** *J. Infect. Dis.* 1958, July–Aug., v. 103, No. 1, 45–51. [23 refs.]

Blood cultures were taken with strict aseptic precautions from children with rheumatic fever and from controls, and incubated for up to 35 days. 66% of 36 children with acute rheumatic fever, who were not having antibiotics, yielded positive cultures. In convalescence and later the proportions were 22 and 9; in febrile controls the percentage was 14 and in non-febrile controls 4. Most of the positive cultures were first recognized after 16–25 days' incubation. 50 "consecutive" isolates were examined for biochemical characteristics; 25 corresponded in all respects to enterococci and 13 others corresponded in most respects. 34 of these 38 strains reacted with a Lancefield group D serum. 7 of the remaining 12 strains reacted with a group A serum, but their characteristics are not described in any detail. *R. E. O. Williams*

Goldring, D., Behrer, M. R., Brown, G. & Elliott, G. **Rheumatic Pneumonitis. Part II. Report on the Clinical and Laboratory Findings in Twenty-Three Patients.** *J. Pediatrics.* St. Louis. 1958, Nov., v. 53, No. 5, 547–65, 22 figs.

This is an important study of rheumatic pneumonitis in children; 23 cases (16 fatal) were seen over a period of 8 years. It is therefore not so rare as is sometimes thought. It may be confused with, but is generally distinguishable from, pulmonary changes associated with congestive heart failure, pulmonary oedema, bacterial pneumonia and viral pneumonitis. The migratory and zonal distribution of the radiographic infiltrations and the effect of antibiotics are pointers in the differential diagnosis. Cardiac involvement seems to be an invariable accompaniment, and residual heart disease a sequela; its appearance is a grave prognostic sign.

It was difficult to evaluate therapy, since all the cases were different, but there was a suggestion that hormone therapy may improve the chance of survival or mitigate the severity of residual heart disease in the survivors. It is felt that in these severe cases hormone therapy at present is indicated. *H. Stanley Banks*

Heart Disease

Morris, J. N. & Crawford, Margaret D. **Coronary Heart Disease and Physical Activity of Work. Evidence of a National Necropsy Survey.** *Brit. Med. J.* 1958, Dec. 20, 1485–96, 3 figs. [70 refs.]

This report is one of a series on the epidemiology of coronary disease of the heart [see, for example, this *Bulletin*, 1955, v. 30, 138: 1956, v. 31, 634] and it continues the study of coronary (ischaemic) heart disease in relation to physical activity of work. The present investigation deals with the frequency in relation to occupation of ischaemic myocardial fibrosis in men dying from causes other than coronary heart disease. The pathologists of 206 hospitals cooperated in the enquiry; each provided particulars of 25 consecutive unselected autopsies on men aged 45 to 70 years no matter what the cause of death or how the case came to autopsy. Macroscopic details were given of any disease in the coronary arteries, its nature, amount and distribution and other relevant details. Although pathologists were asked to give particulars of the last occupation of the deceased this information had to be obtained in many cases from the General Registry Office.

Of the 5,000 reports received, 1,200 concerned deaths from coronary heart disease and thus were excluded from the present enquiry which deals mainly with the presumptive ischaemic cardiac fibrosis found in the 3,800 non-coronary deaths in middle-aged men.

Results showed that the incidence of ischaemic cardiac fibrosis was twice as frequent among workers engaged in light occupations as among those engaged in heavy occupations; large scars (healed infarcts) were found 3 times as frequently among light workers but there was less difference between the 2 groups showing small multiple scars. The excess of large healed infarcts was most evident in the youngest age-group of light workers. Among the hypertensives the prevalence of focal myocardial fibrosis (small multiple scars) was very high in light workers, higher than that found in active and heavy workers with hypertension and much higher than in all those with no record or evidence of hypertension. Those engaged in light occupations showed these small scars about 3 times more often at the age of 45 to 60 than the rest with hypertension and 6 times more frequently than all the others without hypertension. At 60 to 70 years the figures were 1½ times and 3 times respectively.

The pathogenesis of ischaemic cardiac fibrosis may be regarded for the present as coronary insufficiency and the basic pathology is atheroma or atherosclerosis with focal coronary obstruction. Most of the ischaemic scars were associated with topical coronary narrowing; the larger fibrotic patches with complete occlusion. Complete or near complete occlusion was more frequent among those engaged in light work (5·8%) compared with those engaged in heavy work (3·2%). The rate of coronary occlusion was about the same among light workers aged 45–60 years as among heavy workers aged 10 to 20 years older.

The evidence does not suggest that habitual physical exertion materially affects coronary atheroma but there is an indication that it is related to the frequency of coronary occlusion. The main cause of coronary atherosclerosis in man has to be sought elsewhere.

The 3,800 non-coronary deaths of the present enquiry revealed no evidence of any important class factor.

The general hypothesis is stated that the physical activity of work is a protection against ischaemic coronary heart disease. Men engaged in physically active work have less coronary heart disease in middle age, what disease they have is less severe and they develop it later than men engaged in physically less active work.

The main results of the enquiry are said to be that atheroma of the walls of the coronary arteries bears no relationship to the physical activity of occupation; occlusion of the coronary lumen bears some relationship; ischaemic cardiac fibrosis much relationship.

P. A. Clearkin

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order: General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology

INTERNATIONAL CONGRESS ON OCCUPATIONAL HEALTH. XII, Helsinki, 1–6. 7. 1957. **Vol. I. Reports.** 311 pp., numerous figs. 1957. **Vol. II. Summaries.** 151 pp. 1957. **Vol. III. Proceedings.** 622 pp., numerous figs. 1958. [F. mks 4,500 (for 3 Vols.).] Helsinki: Organizing Committee, c/o Työterveyslaitos, Haartmaninkatu 1, Finland.

There is a good deal to be said for an opportunity to meet men and women from other countries who work on similar problems. Whether these fraternal contacts are best achieved against a background of numerous academic papers is not so certain. Most of the lectures could probably be far more easily understood and digested when read quietly in the home study room. The massive range of subject matter here reported is quite startling. The papers delivered by the 31 invited speakers are printed in full in Vol. 1. They are also summarized together with nearly 300 other papers in Vol. 2. This second volume thus enables anyone to skim rapidly through the academic content of the conference. The impression gained is of a vastly ill-assorted, indigestible meal. It is difficult to see what purpose is gained by this volume for many of the summaries are so brief as to amount to no more than the mention of a title. Those papers not appearing in Vol. 1 are printed in full in Vol. 3. In this volume, which is by far the most bulky, there also appears the record of social activities, further attested by some 50 or 60 photographs.

The subjects discussed in the formal sessions included:—

industrial noise
evaluation of invalidity
industrial hygiene norms
human engineering
cardiac patients and work
shift work and health
industrial disabilities of the back
applied psychology and occupational health
occupational non-silicotic pneumopathies
blood diseases in relation to industrial toxicology
isotopes in toxicological research
radiation hazards and prevention
diseases due to stress and strain
industrial nursing.

In the open sessions the subjects included:—

toxicology
pneumoconiosis
other occupational diseases
occupational dermatology
occupational ophthalmology and otology
occupational physiology and psychology
traumatology.

That there was a real international gathering is evidenced by over 1,000 names of those attending from more than 40 countries, and perhaps in this list lies proof of the value of such conferences. Nevertheless, these volumes should not be complacently accepted in this way. Those organizing future conferences should study them carefully with the object of achieving international fraternal contact without mental and physical indigestion. After all, it was a conference on occupational health.

T. O. Garland

PROC. THIRD CONFERENCE INDUST. COUNCIL FOR TROP. HEALTH sponsored by the Harvard School of Public Health, April 16–18, 1957, in Boston. **Industry and Tropical Health, III.** pp. viii + 261, numerous figs. 1957. Boston 15, Mass.: Harvard School of Public Health, 55, Shattuck Street. [$10.00 (Professional Rate $5.00).]

This record of the third conference of the Industrial Council for Tropical Health, sponsored by the Harvard School of Public Health, is produced on lines similar to those of its predecessors, and many of the participants are the same [see this *Bulletin*, 1955, v. 30, 1068].

The papers presented at the 8 sessions were partly related to problems of organization of health services, including educational programmes in preventive medicine and policies for employment, and partly to reviews of certain diseases, malaria, poliomyelitis, dysentery and hepatitis.

The record of organization of medical services by the big oil and other companies is sufficiently impressive, and is brought home in this publication by the facts recorded and the photographs of hospitals and houses reproduced. There seems to be little doubt that these services are efficient and humane, and the policy usually adopted goes beyond the physical care of the workman himself, to make some provision for his family and for education and religious facilities.

For the diseases P. F. RUSSELL surveyed the status of malaria today, indicating the countries of the world where eradication projects are in being, and commenting that these projects in the Americas, Europe and parts of Asia can usually be completed if energetically administered, in spite of resistance to insecticides. G. MACDONALD related malaria to the industrial scene, remarking that industry has often sought undeveloped but fertile land in hot and humid climates, in places which were unpopulated because of malaria or where the clearing of the land produced conditions suitable for the vectors. The efforts made on the tea and other estates of India and elsewhere to control malaria have been very successful, and even in Africa there has been success. R. H. DAGGY contributed a paper on the special problems of oasis malaria in Arabia, where transmission is seasonal and where resistance to DDT has been observed in the important vector *Anopheles stephensi*.

J. R. PAUL discussed poliomyelitis as a tropical problem, showing that it is in fact so heavily endemic in the tropics that the people become immunized in childhood. This means that susceptible adults going to the tropics from countries less saturated are at considerable risk, and for such people vaccination is likely to be indicated. The same author opened a discussion on hepatitis, and at the end of that session DAGGY showed a film on trachoma, prepared by the Arabian American Oil Company as one of a series of education films designed for the Saudi Arabian villager.

The problems associated with selection of personnel for employment in the tropics, and of social adjustment, were dealt with in 2 papers in which the psychological factors were stressed, not only for employees but also for their wives. Other papers related to pulmonary conditions, particularly tuberculosis and its treatment in the employees indigenous to the country in which the industry is located. *Charles Wilcocks*

MAROC MÉD. 1958, Apr. & May, v. 37, Nos. 395 & 396, 323–498; 499–638, numerous figs. [Numerous refs.] **"La Médecine du Travail."**

These two issues of this journal are devoted exclusively to occupational medicine, and the papers have been contributed by French, Belgian and German workers, and though many of them relate to Moroccan conditions, others are more general, or even relate to local conditions in Europe.

The first section contains papers on fatigue, work at high temperatures (as in the deep mines of Belgium), Moroccan miners, rehabilitation, and psychological factors in occupational illness. Of these papers the most detailed is one by A. HOUBERECHTS, F. LAVENNE and J. PATIGNY (*Le travail humain aux températures élevées*, pp. 328–45), in which the various factors are discussed and much experimental work is critically reviewed.

The second section relates to occupational diseases and intoxications, and contains papers on the toxicology of organic phosphorus insecticides, lead, fluorine, manganese (extensively mined in Morocco), cobalt (similarly produced in Morocco), and pyridine. There are also papers on hookworm infection in mines, and on atmospheric conditions in them. Manganism has long attracted the attention of physicians in Morocco, and in the paper by J. RODIER (*Le manganisme au Maroc*, pp. 429–54) there is a bibliography which occupies 3 pages. This paper is illustrated by photographs which show the spasmodic laughter and the motor disabilities which result from the toxic action of manganese on the nervous system.

The second issue of the journal contains a section on pneumoconiosis which opens with a general paper on natural defence mechanisms of the lung, by Professor A. POLICARD, and goes on to other general papers and to some on silicosis in Moroccan mines producing anthracite, phosphates, lead, zinc and other minerals. These papers range widely over the clinical features of the disease.

Succeeding sections relate to accidents at work, legislation and problems related to industrial hygiene. Regulations in force are discussed, and the compensation to be made in the case of accidents and industrial disease.

This collection of papers contains much general information, but will also be a valuable source of knowledge of the industrial scene in Morocco.

Charles Wilcocks

SCHREUDER, O. B. **Place of Routine Examinations in Promotion of Health among Industrial Executives.** *Brit. Med. J.* 1958, Dec. 20, 1506–8.

This paper was presented in the Section of Occupational Health at the Annual Meeting of the British Medical Association at Birmingham in 1958. It is based on the author's experience as a medical director in an American air line and on references to the American literature on industrial medicine. There

is a discussion on the objectives of a health programme with an interesting account of some of the findings at periodic medical examinations carried out during employment and of the value of corrective action which may be taken to treat the disabilities which are discovered. Industrial medicine has "progressed rather rapidly during the past several years in the United States" and "Management has recognized the value of a medical programme in industry, including an executive health programme". It is stated that "an investment in health is good business" and reference is made to a report of the American Management Association which concludes that "from data furnished by a number of industries with medical departments, there is a consistent profit of $3.50 to $5 for each dollar spent in the medical department". *M. E. Delafield*

PATTON, J. L. **The Assessment of Sickness Absence, with special reference to Refuse Collectors.** *Med. Officer.* 1958, Sept. 19, v. 100, No. 12, 193–4.

This valuable paper from the Hendon public health department is an excellent example of one way in which a medical officer of health can ascertain conditions affecting the health of a section of the community for which he has responsibility.

The enquiry began by an examination during one year of the sick-leave certificates presented by any of the Council's staff who had been away from work because of illness for one day or more. The staff were grouped into 9 categories according to the nature of their work, and the illnesses from which they suffered into 13.

Comparison of the figures for each of the 9 grades of staff with those for the Council's service as a whole showed that the refuse collectors had a relatively high incidence of boils and skin infections, arthritis and rheumatism, "diseases of bones and organs of movement" and accidents at work.

This led to a close examination of the refuse collectors' working conditions. As a result, suggestions were made about the best type of protective glove, the best way to lift a heavy dustbin, the provision of non-slip footwear, protection for the shoulders and a protective pad for the quadriceps, the limitation of the weight to be lifted to 130 lb., together with regulations about the maximum size of a bin and the cleaning of dust from the cabs of collecting vehicles by a vacuum cleaner.

Many of these points arose from a careful study of a slow-motion film taken specially to illustrate the exact nature of the work.

[Health departments cannot be expected to be taken seriously in their claims to expand into the field of occupational health unless they take steps to provide a good service for the departments of their own authority.] *Allen Daley*

YAFFE, C. D., JONES, H. H. & WEISS, E. S. **Industrial Noise and Hearing Loss in a Controlled Population—First Report of Findings.** *Amer. Indust. Hyg. Ass. J.* 1958, Aug., v. 19, No. 4, 296–312, 26 figs.

The data reported in this paper are part of the material obtained in the first 4 years of a study on industrial noise and hearing loss by the Occupational Health Program of the U.S. Public Health Service. It was conducted on about 1,600 workers in certain of the factories in 7 Federal penitentiaries. The industries in these factories were metal and wood furniture, clothing, shoes, brushes and cotton and woollen textiles. Audiometric testing of these workers was first carried out at 3-month intervals and later at 3, 6 and 12 months after assignment to a job, and then annually. Eventually all newly admitted inmates, approximately 7,000 in number, were also tested by audiometer at their entrance examination. The mass of data on hearing in relation to sound pressure in the different industries so obtained is described and set out in 26 graphs. "A detailed report of the overall findings is now being prepared. Hearing data for other work intervals should help us to draw some more definite conclusions, particularly if corrections for temporary threshold shift can be made." *M. E. Delafield*

NATIONAL COAL BOARD. **Medical Service. Annual Report 1957** [ROGAN, J., Chief Medical Officer]. 19 pp. [1959.] London: Hobart House, Grosvenor Place, S.W.1.

This is the first annual report of the National Coal Board in which the work of the medical service is described, and it contains a statement of health policy issued in 1957. The aims are to ensure that the worker is fit for his work on entry, that his health is not impaired by his work (if this is possible), that workers who have suffered from accident or illness are given suitable work on recovery, and to carry out research.

These aims involve various examinations of workers, supervision of environment, attention to safety measures, care for the injured, advisory work to managements and workers on resettlement and other problems, organization of research and maintenance of liaison with the National Health Service.

The report deals with pre-employment and other examinations of workers—men exposed to special risks receive special care. Dust conditions in this industry were assessed and the conditions were approved in 84% of power-loaded faces and 93% of hand-filled faces. The number of new certifications fell from a peak of 4,997 in 1955 to 3,756 in 1957 [but the number of men employed is not stated], and in recent years the proportion of men certified whose disability was more than 10% has declined. Beat disease, dermatitis and nystagmus are falling.

The first-aid and ambulance services are in full swing, in collaboration with local authority services, and about 30,000 officials and men have passed a first-aid examination within the last 3 years. Morphia can now be administered to injured workers by specially trained men at a large number of collieries.

By the end of 1957 344 medical centres staffed by nurses had been built and 35 were completed in the year, leaving 70 to be built. Resettlement is largely a matter for the Board's own doctors, and in 1957 18,903 workers with pneumoconiosis were re-employed in the industry. Some details are given of consultations

carried out and on liaisons with the state health service and the universities. At the end of 1957 the Board employed 80 doctors, 363 nurses and 2,454 medical room attendants, 932 of whom were full-time.

Charles Wilcocks

NATIONAL COAL BOARD. **Medical Service. Research on Medical and Allied Problems.** Annual Report 1957 [ROGAN, J., Chief Medical Officer.] 14 pp. [1959.] London: Hobart House, Grosvenor Place, S.W.1.

This short publication consists of a series of abstracts of papers published or in the press, which describe work related to mining medicine and sponsored completely by the National Coal Board, or financed by the Board but carried out by other research organizations, or carried out by outside organizations with collaboration but not financial assistance from the Board.

The subjects include vital and morbidity statistics and the flaws that may be found in their collection; pneumoconiosis field-research in which a long-term investigation is being made of the state of health and the physiological capacity of miners at 25 selected collieries; the study of lung function in pneumoconiosis; the causation of complicated pneumoconiosis by experimental methods in animals; bacteria in mine air; the beat diseases (which are diminishing); epidermophytosis in relation to pit-head baths; breathing apparatus; and the effect of hot and humid conditions.

Research on allied problems includes an investigation of attendance and studies of accidents.

These short accounts are valuable in that they not only indicate the scope of these pieces of work, but give some idea of the main conclusion reached. But of course they are only indications, and the original papers need to be studied.

In this introduction Dr. John ROGAN, the Chief Medical Officer, remarks that the programme of research remains flexible, to meet the new problems likely to arise.

The members of 4 advisory panels are listed—the Epidemiology, Industrial medicine, Physiology and Psychology Panels.

Charles Wilcocks

BURDEKIN, J. T. & DAWES, J. G. **Some Properties of Airborne Dust Clouds in Mining.** *Safety in Mines Research Establishment.* [Portobello St., Sheffield.] *Research Rept.* No. 149, 1958, Oct., 23 mimeographed pp., 16 figs. [2s. 6d.]

Samples of air-borne dust from coal mines have been shown to follow the size-distribution:—

$$dF/dD = Q\alpha \exp(-\alpha D) + (1-Q)\beta \exp(-\beta D)$$

where D is the diameter and α and β are constants (WYNN and DAWES, *Safety in Mines Research Report* No. 28, 1951). An investigation by electron microscopy [CARTWRIGHT and SKIDMORE, this *Bulletin*, 1957, v. 32, 867] revealed that the β term, relating to particles below 1 micron, was due to atmospheric pollution of surface origin borne into the pit in the ventilating air.

In the present paper the first term of the distribution is studied. It expresses the size variation of coal or rock particles whose projected area diameters are between 1 and 10 microns. A fine dust gives a higher value of α than a coarse one.

A large number of samples of coal dust taken at the coal face, in return airways and at loading points in pits all over the country gave mean values of α between 0·34 and 1·33; variations between pits in different parts of the country were apparent, when similar operations gave rise to the dust, but the size distributions were all fitted by the equation satisfactorily. This conclusion held, also, for rock dusts which were finer than the coal dusts. No significant difference in particle size was detectable between clouds of rock dust produced by rotary and by percussive drilling.

Defining the Stokes diameter of a dust particle as the diameter of a spherical particle which has the same density and the same terminal velocity of fall, the shape factor is taken as the ratio of Stokes diameter to the projected area diameter (obtained from microscopic sizing against a graticule).

Particles having a low shape factor penetrate size-selecting devices which operate by sedimentation to a greater extent than more nearly spherical ones. Thus particles having a projected area diameter of 25 microns have been observed issuing from an elutriator which stops 6-micron Stokes diameter particles. It is shown that the assumption of a distribution of values for the shape factor, with a mean of 0·48, enables the acceptance curve of a size-selecting elutriator to be calculated in good agreement with experimental observation.

[It is stated by the authors that the assumption of a certain distribution for the shape factor characterizes the aerodynamic properties of the particles in underground coal-dust clouds. This does not appear to be the case, since the shape factor undoubtedly varies with particle size so that the application of one and the same distribution to all sizes cannot constitute an accurate representation.] *C. N. Davies*

HODKINSON, J. R. **A Note on the Particle-Size Distribution of Microscopic Coal and Rock Dusts.** *Safety in Mines Research Establishment* [Portobello St., Sheffield]. *Research Rept.* No. 153. 1958, Oct., 7 mimeographed pp., 1 fig. [14 refs.] [1s. 3d.]

A simple formula proposed for coal and rock dust size distribution is tested for a number of additional samples. It is shown that the number of particles per unit size interval is equal to $D-D^{-\beta}$ where D is the diameter and β is a constant for a particular dust.

For most air-borne dusts counted by the light microscope on thermal precipitator slides, β varies from 2·1 to 3·1. Higher values are found for coarser particles determined by liquid sedimentation or sieving.

C. N. Davies

GORDIEYEFF, V. A. **Glass Microspheres as Inhalation Tracers.** *Arch. Indust. Health.* Chicago. 1958, Nov., v. 18, No. 5, 389–97, 9 figs. [14 refs.]

Rats, guineapigs and rabbits were exposed to aerosols of glass spheres made by blowing pyrex glass ground

to pass a 325 mesh sieve through a gas flame. The particle size extended down to 0·2 micron diameter and size fractions were separated by impingement. The number and size distribution of particles recovered from the lungs and digestive tract was determined by electron and visual microscopy.

The exposure time varied from 4 to 16 hours and the animals were killed immediately after exposure. No glass spheres were found in the lymphatics but relatively large amounts were recovered from the digestive tract. Particles between 3 and 4 microns diameter were occasionally seen in the alveolar region of rabbits, the smaller bronchi contained many particles from 6 to 7 microns and the main bronchi and trachea carried sizes in the 9 to 12 microns range. The largest particle found in the lower respiratory organs was 23 microns diameter in the main bronchus of a rabbit immediately below the tracheal bifurcation.

A check on total mass retention by particle count was obtained by employing cobalt glass and estimating the cobalt. The work was intended to establish the validity of the techniques rather than to compromise an investigation of respiratory retention.

C. N. Davies

GRASSMANN, A. Trockenfilter zur Luftreinigung. [**Dry Filters for Cleaning Air**] *Staub.* Düsseldorf. 1958, Dec. 1, v. 18, No. 12, 365–6, 5 figs.

Air filters made of synthetic fibres were exposed to the standard test dust of the American Air Filter Institute and the rise in resistance measured as the dust load on the filter built up.

Curves are given for 3 types of filter-medium showing the pressure-air flow relationships when clean and the resistance at a single flow speed for dust loads up to 700 gm./m². Some data on filtration efficiency are given.

C. N. Davies

BRAUER, F. Technische Staubbekämfung in der Grauwackeindustrie. [**Dust Suppression in the Graywacke Industry**] *Staub.* Düsseldorf. 1958, Dec. 1, v. 18, No. 12, 361–3, 4 figs.

Graywacke is a conglomerate of pebbles and sand, found in some parts of Germany, which is used for paving stones. In quarrying operations much dust, containing a high proportion of free silica, may be produced. Hammer drills with hollow steels, through which dusty air is aspirated from the drill tip, are now used to keep the dust concentrations down while the stone is quarried and split; they are electrically operated with ejector-driven air extraction. The ejector is integral with a portable filter container which is connected to the drill by a flexible hose. Working conditions have been improved by providing shelters for the men who trim the stone. Dust produced by stone-crushers is still a problem and filters on extraction ducts tend to clog in wet weather. A new type of filter, in which the elements are continually vibrated up and down to free them of deposit, appears promising.

C. N. Davies

SCHWEIZ. MED. WOCH. 1958, Sept. 6, v. 88, No. 36, 879–82. Abschliessender Bericht der Kommission der Deutschen Gesellschaft für Innere Medizin zur Normung der Nomenklatur und der Symbole von Atmungsgrossen. [**Final Report of the Commission of the German Institute of Internal Medicine on Standardization of the Nomenclature and Symbols of Respiratory Terms.**]

The symbols and definitions are set out in 5 tables. In the main the symbols and abbreviations agree with those used in other countries, and are derived from the Latin or English terms. For instance, the abbreviation for "total" is "tot", not "gesamt", and for "right" is "dex", not "rechts". There are, however, a few divergences.

Charles Wilcocks

CAPEL, L. H. & SMART, J. **Spirometry and Effort Tolerance in Diseases of the Heart and Lungs.** *Lancet.* 1958, Oct. 11, 771–3, 3 figs. [11 refs.]

With the object of assessing the contribution to effort intolerance of heart or bronchial disease where both were present, 534 patients aged 25–65 from the East End of London were graded as to effort tolerance and performance of a forced expiratory volume test (1 second forced expiratory volume × 100 divided by vital capacity).

It is concluded that where both diseases coexist the probability that heart disease is the main cause of moderate or severe effort intolerance increases as the test value exceeds 60% in men or 65% in women. With lower performance of the test, down to 40%, it becomes more probable that "bronchial disease" is the main cause of effort intolerance. There is considerable scatter and overlap in the less disabled patients and the distinction may only be drawn where disability is moderate or severe. "Bronchial disease" included bronchitis, emphysema, asthma and pulmonary fibrosis. The test did not permit distinction between heart disease and pulmonary fibrosis.

M. L. Thomson

CARSTENS, M., BRINKMANN, O., LANGE, H. J., MEISTERERNST, A. and SCHLICHT, H. Beiträge zur Pathophysiologie der Staublungenkrankheit im Bergbau. I. Mitteilung. Über die korrelativen Beziehungen zwischen dynamischen Lungen-funktionswerten und Lebens-und Berufsalter. [**The Physio-pathology of Pneumoconiosis in the Mining Industry. I. Relation of Dynamic Lung Function to Age and Occupation**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 2, 203–26, 11 figs. [19 refs.]

CARSTENS, M., BRINKMANN, O., LANGE, H. J., MEISTERERNST, A. & SCHLICHT, H. Beiträge zur Pathophysiologie der Staublungenkrankheit im Bergbau. II. Mitteilung. Der Geltungsbereich der Sollwerte nach KNIPPING, VALENTIN, VENRATH und BALDWIN, COURNAND, RICHARDS und die dynamischen Lungenwerte von gesunden Bergleuten, Emphysembronchitikern und Silikosekranken. [**The Physio-pathology of Pneumoconiosis in the**

Mining Industry. II. The Range of Expected Values according to Knipping, Valentin, Venrath and Baldwin, Cournand, Richards and Findings for the Dynamic Lung Function Tests in Healthy Miners and those with Bronchitis and Emphysema and Silicosis] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 4, 439–58, 9 figs.

CARSTENS, M., BRINKMANN, O., LANGE, H. J., MEISTERERNST, A. & SCHLICHT, H. Beiträge zur Pathophysiologie der Staublungenkrankheit im Bergbau. III. Mitteilung. Die statischen Lungenfunktionswerte von Bergleuten der Ruhrgebietes. [**The Physiopathology of Pneumoconiosis in the Mining Industry. III. Static Lung Function Tests in Ruhr Miners**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 4, 459–77, 5 figs.

These 3 papers describe ventilatory capacity measurements in 1,000 miners, aged 16–71 years, and with mining experience of 1 to 45 years underground. In the first paper 743 men, some with minor medical or surgical conditions, were considered healthy from the bronchopulmonary aspect and 257 were incapacitated due to silicosis, bronchitis and emphysema or heart and circulatory disorders.

The direct maximum breathing capacity (MBC) and the forced expiratory volume (FEV) were measured with a Knipping spirometer, and the results were compared with expected values calculated according to Knipping's method. The results were found to be related both to age and to the length of time spent working underground. The partial correlations of age, duration of work underground and direct MBC suggested that the decline in MBC with length of working life was greater than that with age. The converse was found in the case of the FEV test except in the men aged 40–49, in whom again the effect of occupation appeared the more important.

Comparison of the mean values found for different age-groups with those expected suggested that the maximum decline in ventilatory capacity occurred 10 years earlier in miners than in other people (aged 40–49 rather than 50–59) and that in them it was also roughly twice as steep.

During the first 10 years of working life, the observed MBC was higher than that expected. A steep decline in ventilatory capacity was observed in the men who had worked 10–24 years underground and whose mean age was 47 years. The authors conclude that the fifth decade is critical for miners not only on account of silicosis but also because of emphysema and bronchitis.

In the second paper the authors first compare the expected direct maximum breathing capacity (MBC) values for 300 miners, first according to Baldwin *et al.*, and secondly according to Knipping *et al.* They show that the expected American values are 30–40 litres higher than the German. The actual measurements of the 300 men approximated more closely to the German expected values and the authors conclude therefore that these have greater validity for studying populations of German miners.

They then re-allocate those men with mild bronchitis, included in their first paper in the healthy group, to their bronchitis group and compare 459 healthy, 279 with bronchitis, or bronchitis and emphysema, 167 with silicosis and 95 with cardiovascular abnormalities. The results of the direct and indirect maximum breathing capacity (MBC) and forced expiratory volume (FEV) for the first 3 groups are given for each 10 year age-group and these are compared with the expected values for the MBC. Up to age 40 the MBC of healthy miners was slightly higher than expected, while over 40 it was lower, being significantly so in men over 50. The bronchitic and silicotic groups showed even greater reductions of the actual from the expected values.

The paper also includes insurance figures indicating that the prevalence of bronchitis and emphysema is significantly higher in miners than in other workers and that among miners it is in fact commoner than all the other accidents and illnesses combined.

In the third paper the authors give their findings in the same group of miners for the vital capacity and its subdivisions. Under 40 years of age the observed vital capacity was significantly higher than expected, while over 40 it was significantly lower. Similarly the observed values were higher than expected for those men who had worked less than 15 years underground but lower than expected in those who had worked for more than 15 years underground. In the bronchitic and silicotic groups the reduction in vital capacity below the expected values occurred earlier and was significantly greater than in the healthy miners. Of the subdivisions of the vital capacity, the complementary air showed a proportionate reduction with age and the reserve air a relatively steeper fall than the vital capacity while the tidal volume remained relatively constant. These findings, broadly similar to those revealed by the dynamic tests, are also attributed to mining.

[The importance of population selection is not considered by the authors.]

[See also this *Bulletin*, 1957, v. 32, 771.]

I. T. T. Higgins

CARSTENS, M., BRINKMANN, O., LANGE, H. J., MEISTERERNST, A. & SCHLICHT, H. Beiträge zur Pathophysiologie der Staublungenkrankheit im Bergbau. IV. Mitteilung. Die Bronchitis der Bergleute. [**The Physio-pathology of Pneumoconiosis in the Mining Industry. IV. Bronchitis of Miners**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1958, v. 16, No. 5, 511–25, 1 fig.

In this long paper there is a detailed account of the examination of 1,000 miners aged from 16 to 71 years by clinical methods, by X-ray and by spirometer measurements with the Aludrin [a preparation of Bochringer, Ingelheim] test. The detailed results of this examination are fully described with tables and there is a long discussion. It was found that 362 of the 1,000 miners had bronchitic signs on auscultation and of these 254 were diagnosed as bronchitis and bronchitis with emphysema, 67 as cases of silicosis

(grades I to III) and 41 as cases of impairment of the heart and circulation. The 638 miners without bronchitic signs were classified as 459 with healthy lungs, 100 as cases of silicosis (grades I to III), 54 as having some disorder of heart and circulation and 25 were diagnosed as bronchitic on their past history. In considering the results some stress is laid on the prominence of bronchial spasm in miners which may be present even in those without diagnostic signs of bronchitis. The opinion is expressed that the dry bronchitis sounds heard on auscultation should not be regarded as unimportant for they are evidence of the reaction of the lungs to dust. It is also believed by the authors that adequate care and timely removal from work of a dusty nature of miners with emphysema and bronchitis will yield far better results than in miners with developed silicosis. Having regard to this view silicosis is in no way the chief health problem in mining workers. *M. E. Delafield*

FURUKAWA, M. [**Studies on Transition of Silicosis and Silicotuberculosis at Matsuo Mine** (Rep. 4). **Part IV. Silicosis and Cardio-Pulmonary Function.**] *J. Sci. of Labour.* Tokyo. 1958, Oct., v. 34, No. 10, 842–60. [10 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"One hundred and sixty-six workers with silicosis, group A of 96 patients and group B of 70 were observed during 8 and 4 years respectively.

"1) In case of the progressive silicosis the breathing cessation time was shortened but in case of the invariable silicosis it was constant.

"2) There was a significant relationship between the vital capacity and the progressive grade of silicosis.

"3) Any correlation was not observed between the pulmonal function and the progressive grade of silicosis in both groups A and B.

"4) There was no relationship between the ventilation capacity and the progressive grade of silicosis in both groups A and B.

"5) Statistically there was no significant relationship between the change of respiratory rate after a load test and the progressive grade of silicosis.

"6) There was no significant relationship between the change of the pulse rate at rest as well as after the load test and the progressive grade of silicosis.

"7) In case of the progressive silicosis, a significant difference was observed between the blood pressure and the progressive grade of silicosis, but in case of the invariable silicosis was not observed."

KING, E. J., YOGANATHAN, M. & NAGELSCHMIDT, G. **The Effect of Diamond Dust alone and mixed with Quartz on the Lungs of Rats.** *Brit. J. Indust. Med.* 1958, Apr., v. 15, No. 2, 92–5, 5 figs.

This investigation comprised 5 experiments:—
(1) 100 mgm. diamond dust,
(2) 2 mgm. quartz dust,
(3) 5 mgm. quartz dust,
(4) 100 mgm. diamond dust + 2 mgm. quartz dust,
(5) 100 mgm. diamond dust + 5 mgm. quartz dust.

The particle size of the dusts was in the range of 0·08–3·6μ and the percentage distribution of the particles by number and size was determined and is tabulated. 7 male rats (black and white MRC strain) were used in each experiment. The dusts were suspended in physiological saline and injected intratracheally. The duration of the experiments was 400 days during which some rats died and the others were killed at intervals after 200, 300 and 400 days. The pathological results were assessed histologically according to the 5 grades of increasing fibrosis defined by BELT and KING [this *Bulletin*, 1945, v. 20, 776] and restated in the article.

After 400 days diamond dust alone gave rise to no fibrosis, but quartz alone produced fibrosis, 5 mgm. being more productive than 2 mgm. When 5% of quartz was combined with diamond dust, lesions were more numerous and slightly more fibrotic than with quartz alone. The authors conclude that the effect of diamond dust and varying amounts of quartz is to produce more pathological response than either of them alone; and as with coal, the effects of the combined dusts are greater than the apparent sum of each separately. As intratracheal injection of dusts does not represent natural methods of entrance of dust to the lungs, further experiments are planned to determine whether these conclusions are valid when the dust is administered by inhalation. *A. Meiklejohn*

KING, E. J., ZAIDI, S., HARRISON, C. V. & NAGELSCHMIDT, G. **The Tissue Reaction in the Lungs of Rats after the Inhalation of Coal Dust containing 2% of Quartz.** *Brit. J. Indust. Med.* 1958, July, v. 15, No. 3, 172–7, 4 figs. [19 refs.]

Animal experiments have shown that anthracite coal dust produces only minimal fibrosis of the lungs [this *Bulletin*, 1945, v. 20, 776]. To find out whether a small amount of silica mixed with pure anthracite coal would induce fibrosis the following experiment was carried out.

A group of 30 male rats, average weight 150 gm., were exposed in a dusting cabinet over a period of 500 days to the inhalation of a low concentration of quartz; all particles were under 10μ in diameter.

A second group of rats were similarly exposed to a comparable dust composed of an intimate mixture of South Wales anthracite coal and 2% quartz.

The animals dusted with the low concentration of quartz alone showed no evidence of fibrosis in the lungs or lymph nodes. In the rats dusted with the mixture of anthracite and quartz discrete dust foci developed in the lungs and lymph nodes, but without showing any evidence of fibrosis in the lungs and only a little in the lymph nodes. Chemical analysis of the ash of lungs revealed the interesting fact that the amounts of silica in the quartz only group of rats was much less than in those dusted with anthracite plus quartz, despite the "quartz particle hours" of dusting being roughly similar. *A. Meiklejohn*

NAGELSCHMIDT, G., NELSON, E. S., KING, E. J., ATTYGALLE, D. & YOGANATHAN, M. **The Recovery of Quartz and other Minerals from the Lungs of Rats; a Study in Experimental Silicosis.** *Safety in Mines Research Establishment.* [Portobello St., Sheffield.] *Research Rept.* No. 146, 1958, May, 28 mimeographed pp., 7 figs. [16 refs.] [3s. 0d.]

During recent years the authors have tried to devise and develop animal experiments, which would provide a reasonably accurate quantitative measure of the fate of various dusts, when introduced into the lungs [see, for example, this *Bulletin*, 1953, v. 28, 830]. It was found possible to inject intratracheally measured quantities of suspensions of dusts of known chemical composition and size. Thereafter investigations were made to discover by analyses of the lungs and lymph nodes what proportion of the injected dust could be recovered after different time intervals. The fibrogenic power of the individual dusts was determined by histological examination. The dusts were suspended in Ringer solution, sterilized and injected intratracheally. The authors recognize that this technique does not represent " physiological " conditions.

The object of the present series of experiments was to obtain balance sheets for different materials injected into the lungs of rats; to discover if there were any differences in the rates of removal of fibrogenic and non-fibrogenic dusts; and to test the silica solubility theory of silicosis.

The animals used were rats (black and white M.R.C. strain). Materials tested were calcined flint, quartz (Belgian glass sand), corundum (Al_2O_3), anthracite and bituminous coal, and radio-activated tantalum (^{182}Ta) carbide and scandium (^{46}Sc) oxide. Size of prepared particles was in the range of under $0{\cdot}5\mu$ to 8μ. Stokes diameter. According to the purpose of the separate experiments the rats were killed at intervals from immediately after injection up to 1 year.

The ratio of volume to surface diameter of samples was determined by projection counting under the electron microscope and quartz ratings by Geiger-Müller diffractometry. Silica solubility was measured in buffered Ringer solution at 37°C.

In view of the importance and interest of this study the authors' summary is reproduced:—

" In the course of pneumoconiosis research the recovery of a number of dusts injected into rats' lungs was studied by determining the amounts retained in lungs and lymph nodes at different times, up to 1 year after injection.

Two experiments with five flint fractions of graded size (below $0{\cdot}5\mu$ to 8μ), which had been injected at constant surface showed, between 3 and 12 months after injection, constant total recoveries of the order of 55 per cent of the amounts injected for the four larger fractions ($0{\cdot}5\mu$ to 8μ); a lower total recovery of the order of 40 per cent was obtained for the smallest fraction (below $0{\cdot}5\mu$).

Recoveries of highly fibrogenic quartz and of almost inert corundum of equal size were studied in three experiments. Except for the first 2 months after injection, the total recoveries of both materials were equal, dropping after 3 months to about 60 per cent and thereafter remaining constant up to 1 year. The amounts of dust in the lymph glands increased with time, and after 1 year 28 per cent of the total quartz recovered was in the lymph glands as against 16 per cent of the corundum.

A comparison of the properties of quartz isolated after different time intervals from the lungs showed that a loss of a small percentage had occurred because of solubility; reasons are given why the dissolution of silica is thought not likely to be the controlling factor in fibrogenesis.

Recoveries of anthracite and bituminous coal dusts showed no clear difference between the two coals. The total recoveries as a function of time were very similar to those of quartz and corundum; after 1 year the proportion of dust in the lymph glands was 10 per cent, somewhat lower than for corundum, and considerably lower than for quartz or flint of similar size.

In two pilot experiments with labelled tantalum carbide and scandium oxide, recoveries were measured by Geiger-Müller counting technique. The results were very different, tantalum carbide being rapidly lost from the lungs and scandium oxide only very slowly.

The gravimetric work which was based on more than 300 analyses showed that all dusts of comparable size gave very similar total recoveries, irrespective of their fibrogenic activity. After a period of rapid loss of dust during the first 2 months, probably due to removal via the bronchi, there was no further measurable loss, but continued movement of dust from the lungs to the lymph glands took place. Fibrogenic dusts were transported more than inert dusts. With fibrogenic dust (flint) size was important: the smaller the size of the flint, the higher was the proportion that went to the lymph nodes, and the earlier did it get there."

With reference to the silica solubility theory of silicosis the conclusion is that the flint experiments suggest that there is no direct relation between solubility and pathogenic activity. *A. Meiklejohn*

MOSINGER, M., FIORENTINI, H., EL FEKI, M. & CARTOUZOU, G. Sur le métabolisme de la silice après administration intrapéritonéale de fortes doses de quartz. [**Metabolism of Silica after Intraperitoneal Administration of High Doses of Quartz**] *Arch. Malad. Professionnelles.* Paris. 1957, Nov.–Dec., v. 18, No. 6, 802–5.

The purpose of this investigation was to study the concentration of silica in the organs of rats and guinea-pigs after intra-abdominal injection of different quantities of silica. Quartz was administered suspended in normal saline. The animals were killed at intervals after the final injection. Estimations were made of the silica content of the various organs; results are expressed in grammes per kilogramme weight of organ.

Only in some of the animals was silica detected in the organs within 24 hours of injection. In others there seemed to be a latent period of about 24 hours. Thereafter silica was present in all the organs examined; in the liver, kidneys, lung, brain, heart and particularly

in the spleen. The optimum dose for such a study is given as about 5 gm. per kgm. of body weight.

A. Meiklejohn

GROSS, P., WESTRICK, Marian L. & MCNERNEY, J. M. **Progression of Experimental Silicosis in the Rat.** *Amer. Indust. Hyg. Ass. J.* 1958, June, v. 19, No. 3, 201–4, 8 figs.

The authors consider that distinction should be made between "activity" and "progression" of the silicotic process. They define "activity" as the presence of granulation tissue or immature connective tissue and "progression" as continuation or resumption of the silicotic process after exposure to silica dust has ended. The pathological features of progression were studied in a series of animal experiments. Silicosis was produced in separate groups of rats by inhalation of quartz dust, by intratracheal injection of quartz, and by intratracheal injection of flint. The animals were allowed to survive 6 to 9 months after exposure to, or administration of the dust. Histological observations of the lungs showed immature cellular silicotic nodules at the periphery of mature nodules. Collagenization of alveolar walls was not frequent. There were occasional intra-alveolar nodules consisting mainly of macrophages and their débris with only a little reticulin and collagen. Incineration studies showed concentrations of silica particles in all the immature foci whereas only scanty particles were present in mature foci. [No evidence is provided to differentiate the histological features of "progression" from those of "activity"].

D. Rivers

KERSTEN, W., KRISCH, K. & STAUDINGER, H. Untersuchungen zum Silicoseproblem. Über den Einfluss von oligomerer Kieselsäure auf die oxydative Phosphorylierung. **[Studies on Silicosis. Effect of Silicic Acid on Oxidative Phosphorylation]** *Hoppe-Seyler's Ztschr. physiol. Chem.* 1958, v. 313, 109–16, 1 chart. [Refs. in footnotes.]

The English summary appended to the paper is as follows:—

"1. In a concentration of 10 mg% SiO_2 (= $1{,}67 \cdot 10^{-3}$ M), oligosilicic acid causes a lowering of the P/O quotient of rat liver mitochondria in vitro.

"2. Under similar conditions, the utilization of β-hydroxybutyrate is inhibited about 17% in comparison to a 30% inhibition of the assimilation of phosphate by SiO_2.

"3. The ATPase activity of mitochondria is not influenced by oligosilicic acid.

"4. 10 mg% SiO_2 causes a pronounced stimulation of the swelling of mitochondria."

VIGLIANI, E. C. & PERNIS, B. **Immunological Factors in the Pathogenesis of the Hyaline Tissue of Silicosis.** *Brit. J. Indust. Med.* 1958, Jan., v. 15, No. 1, 8–14. [52 refs.]

The various hypotheses, mechanical, chemical and physical, which have been advanced to explain the initiation and development of silicosis, have all, in some measure, proved inadequate. In the main, the studies of pathogenesis of the disease have concentrated on the seed, namely, the minute crystals of free silicon dioxide. But the range and variety of clinical and pathological changes observed among workmen apparently exposed to almost identical risks have long suggested that the soil, the individual organism, could not be excluded from consideration. Accordingly to fill gaps in the hypotheses recourse was had to such imprecise factors as "predisposing causes" and infection, notably tuberculous infection. Recognition of interaction of seed and soil has recently led to increased consideration of a possible immunological basis of the pathogenesis of the disease. Relative to this the following facts require note.

Collagen is the characteristic constituent of the fibrous tissue of the silicosis nodule. Silicosis may thus be regarded as a collagen disease and at present an immunological pathogenesis is ascribed to this group of diseases.

In silicosis there is almost invariably an increase of serum gamma globulins and sometimes also of alpha and beta globulins. These blood protein changes are associated with an increase in globulin-producing parenchymal cells in certain tissues. Silicotic hyaline tissue also differs in many respects from other physiological and pathological hyaline tissues, such as scar tissue. Whereas true connective hyaline consists almost entirely of collagen fibres, silicotic hyaline is composed of 40% collagen, the remainder being globulin, which must be considered as having an intermediate position between serum beta and gamma globulin. In addition silicotic hyaline tissue contains carbohydrate to the extent of about 3% of the total amount of the protein, and lipids to 20%. From a biochemical point of view silicotic hyaline tissue is very similar in its globulin, carbohydrate and lipid content to amyloid substance, for which an immunological pathogenesis has been accepted by many pathologists. It is inferred that silicotic hyaline is a reticular structure within which serum globulins have precipitated.

To cover these observations the authors advance the hypothesis that the genesis of the fibro-hyaline tissue of silicosis is due to an antigen-antibody reaction—that is to say it is in the nature of an immunological reaction. The details of the precise mechanism of the reaction have not been fully elucidated. It is suggested that silica retained in the lungs could itself give rise to a slow but prolonged production of antigens. This mode of action would cover the long latent period in the insidious onset of the disease. Direct damage to cells by silica could lead to the development of auto-antigens.

Silica could also act as a booster of hetero-antigens, such as those of bacterial origin, particularly the tubercle bacillus. For this there is some experimental support and this action would help explain the problem of the development of massive hyaline fibrosis. Finally auto-antigens might be liberated indirectly from depots of dust such as occur, for example, in the hilar lymph nodes.

[Apart from the hypothesis, this contribution helps to underline the great importance of fundamental as opposed to field research in the study of the dust diseases of the lungs.] *A. Meiklejohn*

MOSINGER, M. Sur les altérations vasculaires dans la silicose pulmonaire. Nodules silicotiques périvasculaires. [**Vascular Changes in Pulmonary Silicosis. Perivascular Silicotic Nodules**] *Arch. Malad. Professionnelles.* Paris. 1957, Nov.–Dec., v. 18, No. 6, 776–81, 7 figs.

Many observers have recorded the occurrence of pathological lesions in the pulmonary blood vessels in cases of silicosis. Consideration of these changes is important in relation to cardiac manifestations in patients suffering from silicosis.

A careful study of these vascular lesions was carried out in 12 cases of human silicosis. A variety of changes, classified in 6 groups, were observed in the arteries and veins, involving the various coats of the vessels separately and in combination. Some silicotic nodules started outside the vessel, which they ultimately surrounded completely. Vascular lesions do not always accompany silicosis and cor pulmonale is not dependent on their presence. *A. Meiklejohn*

MARKS, J., JAMES, Dinah M. & MORRIS, T. G. **The Treatment of Experimental Silicosis with Compound 48/80.** *Brit. J. Indust. Med.* 1958, Jan., v. 15, No. 1, 1–7, 5 figs.

In 1957 Marks [this *Bulletin*, 1958, v. 33, 592] reported that compound 48/80, an organic base used experimentally as a histamine liberator, protects phagocytic cells in tissue culture against the toxic effect of silica dust. The degree of protection observed appeared sufficiently high to merit a study of the drug's activity in laboratory animals. Mice were used because of their relatively low susceptibility to histamine and because a convenient technique was available for producing silicosis in them [this *Bulletin*, 1956, v. 31, 722]. Each mouse received a single dose of 0·5 ml. suspension of tridymite-silica-dust. Some mice died almost immediately after dust injection; the survivors were allotted to experimental groups at random.

A few hours after the dust injection, groups of mice were treated by intraperitoneal injections of compound 48/80 according to defined dosage schedules and killed between 2 and 3 months later. The amount of silicosis induced was assessed by histological examination of the liver and by estimation of its collagen content. A considerable degree of protection against the effect of the dust is claimed for compound 48/80. *A. Meiklejohn*

KNEIDEL, H. Die Differential diagnose von Silikose und Tuberkulose. [**The Differential Diagnoses of Silicosis and Tuberculosis**] *Ztschr. f. ärztl. Fortbildung.* 1958, Nov. 1, v. 52, No. 21, 896–902. [73 refs.]

A capable review on and around the subject.
I. T. T. Higgins

MORETTI, E., COSTA, G. & PAOLI, G. Il valore della determinazione della proteina reattiva C nel siero degli ammalati di silicosi e di silico-tubercolosi. [**The Value of C-Reactive Protein Estimation in Silicosis and Silico-Tuberculosis**] *Lotta c. la Tubercolosi.* 1958, Aug.–Sept., v. 28, Nos. 8/9, 851–9. [31 refs.]

The authors' summary may be translated as follows:—

The authors estimated the C-reactive protein and the erythrocyte sedimentation rate in 289 subjects with various forms of silicosis or silico-tuberculosis; in most cases the C-reactive protein test was positive at high titre in cavitated or exudative silico-tuberculosis, positive at medium titre in silicosis associated with miliary tuberculosis and in the conglomerate form, but mostly negative in nodular and reticular silicosis. They discuss the significance of these results and conclude that the test can be used in differential diagnosis of these forms in addition to other diagnostic procedures.
Charles Wilcocks

LÖBLICH, H. J., KOCH, W. & NORDMANN, M. Die Resorption einverleibten Staubes. Die Aufnahme von Kieselgur. [**The Absorption of Assimilated Dusts. Absorption of Kieselguhr**] *Beiträge z. Silikose-Forschung.* 1957, No. 50, 11–52, 14 figs. [13 refs.]

Kieselguhr was produced either by baking diatomaceous earth in a kiln or by calcining it at 125° Celsius. The resulting dust was suspended in Tyrode solution and was injected in the mesentery of the rabbit. *In vivo* observations as well as histological sections showed the dust to be rapidly dissolved. Most of the dust disappeared without producing any permanent local tissue reaction. Giant cells were seen to ingest and destroy the diatoms and only a small amount of dust entered the lymphatics and lymph nodes.

The results are also given of experiments with kieselguhr administered to the free peritoneal cavity, to the cornea of the rabbit's eye and to the lungs (by both inhalation and intratracheal injection). No granulomata were produced by any of these methods and there was little difference to be observed between the crystalline and non-crystalline forms of the dust.

Observations were made during the few hours after administration of the dust and at various intervals up to 5 months. *D. Rivers*

KING, E. J., YOGANATHAN, M. & NAGELSCHMIDT, G. **Tissue Reactions produced by Calcium Fluoride in the Lungs of Rats.** *Brit. J. Indust. Med.* 1958, July, v. 15, No. 3, 168–71, 4 figs.

22 male rats of the black and white Medical Research Council strain (average weight 200 gm.) were each injected intratracheally with 50 mgm. of calcium fluoride. The dust was prepared by grinding water-clear colourless crystals of calcium fluoride to a fine powder, which was water-sedimented to give a 0·5–2μ fraction, mean particle size 1μ. For injection the powder, which contained less than 0·1% of silica, was suspended in physiological saline.

During the course of the experiment 8 rats died between 39 and 207 days after injection. Those dying during the first 90 days showed evidence of bronchopneumonic consolidation and widespread necrosis,

which on bacteriological investigation did not reveal the presence of organisms. 13 rats were killed at intervals between 30 and 365 days after injection [only 21 rats out of 22 stated to be in the group are accounted for in table 2 of the article, but this does not affect the results of the experiment]. The lungs were dissected out carefully, examined histologically with special reference to reticulin and collagen, and the collagen content determined by chemical analysis. The results were measured against those of a previous experiment [STACY and KING, this *Bulletin*, 1954, v. 29, 1067] in which a group of rats were similarly injected with 50 mgm. of quartz. Calcium fluoride produced fibrosis but its fibrogenic capacity was considerably less than that of quartz. *A. Meiklejohn*

SÜSSMAIER, A. Die Erfahrungen beim Einsatz von Frischluftmasken in Steinmetzhallen. [**Experience with Air-Line Respirators for Stone-Masons**] *Staub*. Düsseldorf. 1958, Dec. 1, v. 18, No. 12, 363–4, 2 figs.

Oro-nasal respirators fed with clean air were tried out by stone-masons over a period of years and were found not to interfere significantly with their work. Air pressures and flows are not given.

C. N. Davies

ELKINS, H. B. **Labeling Requirements for Toxic Substances. The Governmental Industrial Hygienists' Viewpoint.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 451–6, 1 fig.

"In 1957, the Committee on Standard Labeling Procedures of the American Conference of Governmental Industrial Hygienists prepared a guide to rules and regulations for the labeling of hazardous substances." Copies of the guide were sent to all members of the Conference and to various trade associations. Without exception the industrial groups registered protests against the guide which ranged from specific criticisms to the "blunt suggestion" to leave "the handling of labeling to people who knew something about it."

In this article some of the differences in viewpoint are reviewed. A history of precautionary labelling of industrial chemicals is shortly described. About 25 years ago the Surgeon General of the United States Public Health Service "negotiated some gentleman's agreements" as a result of which the Manufacturing Chemists Association (MCA) developed a logical system of labelling and issued a manual on this. This manual "is the most useful document currently in existence dealing with warning labels". It is an excellent manual but it and the various State regulations based on it "contain certain trends and inconsistencies that are objectionable, in my opinion, to those of us interested primarily in the health of industrial workers".

The objections to the MCA manual which are described at considerable length concern particularly 2 trends which are "a shift in emphasis toward accident, rather than health hazards" and "to place almost the entire emphasis on pure substances, and to mention mixtures, in most cases, only in passing".

Tribute is paid to the "tremendous job the MCA has done in the promotion of adequate precautionary labeling." The Guide adheres closely to the labelling principles of the MCA manual but deviates from those principles where it was felt to be necessary "to protect the interests of industrial workers or to make regulations more workable". *M. E. Delafield*

LEWIS, C. E. **A Method for Reporting Toxicological Information.** *Arch. Indust. Health.* Chicago. 1958, Dec., v. 18, No. 6, 457–9, 1 fig.

In this short paper which is abstracted from a dissertation the author refers to the "number of independent variables in a single test of toxicity that defy correlation" and to the disadvantage of determining the MLD, LD or LD50 which "cannot be expressed in terms of one another, except in the confines of a single experiment". There is then a description of the method of measuring the dose of a metal, under investigation for its toxicity, in terms of milliequivalents per litre which takes into account the valency of the metallic ion. This method has been used only fairly recently in clinical medicine in the study of fluid and electrolyte metabolism to replace the measurement of milligrammes per cent. To make the conversion from milligrammes to milliequivalents, the actual weight of the metallic ions administered is divided by the equivalent weight of the element which is its atomic weight divided by the valency.

A table sets out a comparison of the order of toxicity of metallic ions as determined by the 2 methods of dosage measurement. Definite differences in the relative positions of the several ions and in their grouping exist in the 2 scales. These differences are discussed.

"The reporting of toxicity data in terms of milliequivalents or millimoles would seem to be an inevitable sequel to the acceptance of a molecular basis of toxicology." *M. E. Delafield*

DECKER, Lucille E., BYERRUM, R. U., DECKER, C. F., HOPPERT, C. A. & LANGHAM, R. F. **Chronic Toxicity Studies. 1. Cadmium administered in Drinking Water to Rats.** *Arch. Indust. Health.* Chicago. 1958, Sept., v. 18, No. 3, 228–31.

The toxicity of cadmium from inhalation of cadmium oxide or cadmium sulphide fumes in certain industries has been well established and experimental studies in which cats and dogs were similarly exposed have also shown cadmium to be toxic. In addition, acute cadmium poisoning has been caused by contamination of food in contact with utensils plated with this metal. Toxicity of orally administered cadmium chloride has been reported in several animal experiments, and the influence of diet on toxicity has been studied. Rats receiving 50 parts per million (p.p.m.) cadmium in water exhibited reduced blood haemoglobin and stunted growth when compared with rats receiving the same amount of cadmium in their food. The present study was undertaken to investigate the effects of long-term ingestion and retention of cadmium in tissues at low-intake levels such as might be encountered in water supplies.

5 groups of rats were given water containing between 0·1 p.p.m. and 10 p.p.m. cadmium for 1 year. No difference between these groups and controls were observed in water intake, food consumption or body weight. nor were any pathological changes in blood or other tissues noted. Cadmium content of either liver or kidney increased in direct proportion to the cadmium intake. Kidneys retained 2 to 3 times the amount of cadmium retained by the liver when calculated as microgrammes of cadmium per gm. of fresh tissue. Tissue values obtained at the end of a year's ingestion were roughly double those obtained at the end of 6 months. A reduction in growth rate, water consumption and blood haemoglobin was found in rats ingesting 50 p.p.m. cadmium for 3 months. Bleaching of incisors was also observed in these animals. *P. J. R. Challen*

MacKenzie, R. D., Byerrum, R. U., Decker, C. F., Hoppert, C. A. & Langham, R. F. **Chronic Toxicity Studies. II. Hexavalent and Trivalent Chromium administered in Drinking Water to Rats.** *Arch. Indust. Health.* Chicago. 1958, Sept., v. 18, 232–4. [13 refs.]

Acute toxicity to chromium by topical exposure or inhalation resulting in ulcer-like lesions has been recognized as an industrial hazard for many years. Although acute poisoning by ingestion is well documented, few investigations have been made on the chronic toxicity of ingested chromium. The extensive industrial use of chromium and disposal of chromium wastes has resulted in contamination of many water supplies in the United States. This paper reports a study of the hazards of prolonged ingestion of small amounts of chromium.

5 groups of rats were given water containing between 0·45 and 11 p.p.m. of chromium as chromate ion for a year. No differences were observed between these groups and the controls as to water intake, food consumption or weight gain; nor did an analysis of blood at monthly intervals or examination of tissues at 6 months or a year show any significant differences between any of the groups given chromium and the control group. There was an abrupt rise in tissue chromium concentration (kidney, liver, femur and spleen) when rats ingested water having concentrations above 5 p.p.m. of chromate ion. 2 groups of rats were given water containing 25 p.p.m. of chromium as hexavalent and trivalent chromium, respectively, for 1 year. No toxic symptoms were observed in either group. However, tissue concentrations of chromium were approximately 9 times higher in the group given hexavalent chromium. *P. J. R. Challen*

Graham, J. C. **Unsuspected Benzene Contamination in a Can-Making Process.** *Trans. Ass. Indust. Med. Officers.* 1958, Oct., v. 8, No. 3, 86–93, 6 figs. Discussion 93.

It will come as a surprise to many that 500 gallons of benzene are used each week in a well-known canning factory. It serves as a solvent for the rubber film that makes the air-tight seal when the can end is fused to the can body. The process of mixing the solution and its application by machines to the cans is described and illustrated.

No operator had shown or complained of any symptoms suggestive of intoxication over the past 10 years. However, in 1951 a routine blood count of the man mixing the solution showed a suspiciously low white count and he was taken off the job for a time. In 1954 after he had returned he again had to be rested. In 1955 the new operator also showed a fall in his white count and this served as the stimulus for a very careful investigation as to what happened to the benzene in the factory, not only officially but unofficially as it were (degreasing a floor, cleaning paint brushes etc.). Air estimations of benzene were made in the mixing shed at various stages and in a number of places, revealing that at certain times concentrations became high. Subsequent action to protect the man is described.

[This is a very frank helpful paper admirably demonstrating the detailed care needed to safeguard the odd man in some large concern who handles a toxic substance away in an obscure corner where his behaviour and working details can so easily go unnoticed for years.]

Dr. Ethel Browning in the discussion said that in her view any worker exposed to benzene showing a total white count below 5,000 should be regarded with suspicion. *T. O. Garland*

Elsea, J. R. & Paynter, O. E. **Toxicological Studies on Bis (Tri-*n*-Butyltin) Oxide.** *Arch. Indust. Health.* Chicago. 1958, Sept., v. 18, No. 3, 214–17.

Bis (tri-*n*-butyltin) oxide is a colourless to slightly yellow liquid (sp. gr. 1·17) which is finding widespread use in the paper industry for control of slime in water systems, and the general control of bacteria and fungi in allied industrial applications such as wood preservation. The authors have conducted acute and subacute toxicity studies in rats, rabbits and guineapigs which indicate that this compound is a moderately toxic material. It was ascertained that the acute oral LD50 for male albino rats is 194 mgm./kgm. and 148 mgm./kgm. when administered in aqueous and oil media, respectively. When bis (tri-*n*-butyltin) oxide was fed in the diet to groups of male albino rats, all the test animals exhibited growth suppression during the experimental period, the suppression increasing in severity with increased feeding levels. The acute dermal LD50 for albino rabbits is about 11·7 gm./kgm. A single application of the undiluted material produced a moderate degree of dermal irritation and there were gross signs of systemic toxicity from skin absorption. 5 daily applications of a newsprint type of paper containing 8·0 parts per million of bis (tri-*n*-butyltin) oxide to the skin of rabbits produced no gross evidence of dermal irritation or systemic toxicity. It was not possible to determine conclusively whether the compound is capable of inducing skin sensitization.

The evidence collected from these studies indicates that precautions should be observed to prevent ingestion or dermal contact when handling this material. *P. J. R. Challen*

PFITZER, E. A., YEVICH, P. P., GREENE, E. A. & JACOBSON, K. H. **Acute Toxicity of Red Fuming Nitric Acid-Hydrofluoric Acid Vapor Mixture.** *Arch. Indust. Health.* Chicago. 1958, Sept., v. 18, No. 3, 218–21.

Red fuming nitric acid (RFNA) is an important oxidizer in high-energy propulsion. It is highly corrosive, and causes severe local damage on cutaneous contact or on inhalation of its vapours. It presents storage problems, not only because of its corrosive nature, but also because of the pressure increase in storage drums. The addition of small amounts of hydrofluoric acid decreases the storage problems of RFNA. However, this raises questions about possible changes in toxic properties. It did not seem likely that the small amounts of hydrofluoric acid present would significantly affect the highly corrosive properties of RFNA on skin, but some change in vapour toxicity was anticipated. Therefore a study of the toxicity of the vapour mixture in rodents was undertaken.

In a recent study of the toxicity of RFNA vapours GRAY and his associates [this *Bulletin*, 1955, v. 30, 328, *ter.*] concluded that the primary toxic constituents of these vapours is nitrogen dioxide (NO_2) and that the nitric acid component played only a minor role. The primary toxic action was production of pulmonary oedema.

As a result of their experiments the authors conclude that the addition of up to 0·5% hydrofluoric acid to red fuming nitric acid does not significantly alter the acute toxicity of the vapours. The production of pulmonary oedema is the main danger from their inhalation. Vapours from the acid mixture containing about 0·1% hydrofluoric acid have an odour similar to NO_2, and have the same median level of detection (8 p.p.m.). The odour should serve as adequate warning to most men of the presence of acutely dangerous concentrations. *P. J. R. Challen*

DARKE, C. S. & WARRACK, A. J. N. **Bronchiolitis from Nitrous Fumes.** *Thorax.* 1958, Dec., v. 13, No. 4, 327–33, 8 figs. [17 refs.]

Nitrous fumes are particularly dangerous in that though they may cause severe damage, the immediate effect is minimal. They are relatively insoluble in water and hence it is some time after inhalation before inflammation in the bronchioles and lung oedema develop.

2 cases are described, 1 of them fatal. The latter was a man aged 24 who caught strong nitric acid from a leaking rubber bucket in an ordinary galvanized one. He was exposed to the resultant fumes for under a minute, finished the shift without complaint, but at home developed a distressing cough with frothy mucoid sputum. A doctor was not called for a week, he was admitted to hospital after a further week and died a few hours later. Necropsy findings are described and illustrated. He died from bronchiolitis secondary to the irritation from nitrous oxide fumes.

The second patient was an electroplater, aged 59, admitted to hospital 17 days after exposure to the fumes resulting from stripping cadmium-lined bolts in a mixture of nitric acid 1 part and sulphuric acid 4 parts. It is of particular interest that this was done outside in the open yard. 7 days after exposure his voice became husky and his chest felt tight; gradually incessant coughing developed with much frothy, occasionally blood-stained sputum. He became very distressed, restless and cyanosed.

When seen in hospital he was diagnosed as suffering from bronchiolitis; investigations carried out are described. He had a mild fever for 3 days and was treated with chlortetracycline (2 gm. daily for 5 days, followed by 1 gm. daily for 7 days). With the purpose of limiting scarring, cortisone was given (150 mgm. the first day and 100 mgm. for 5 days thereafter with gradual withdrawal over 8 days). Eventually there was complete recovery.

There follows a useful discussion on the oxides of nitrogen and the processes in which they may present a hazard, and an account of clinical symptoms, pathology and treatment. *T. O. Garland*

AMDUR, Mary O. **The Respiratory Response of Guinea Pigs to Sulfuric Acid Mist.** *Arch. Indust. Health.* Chicago. 1958, Nov., v. 18, No. 5, 407–14, 6 figs. [15 refs.]

Sulphuric acid in the atmosphere is held to be responsible for the mortality that is associated with dense smog in cities. This acid is also met with as a mist in many industrial occupations.

Guineapigs are more sensitive than mice, rats or rabbits. In the present investigation they were exposed to 3 different mists with particles sized 0·8 μ, 2·5 μ and 7 μ, respectively, in concentrations of 2–40 mgm./cu. m. for periods of 1 hour.

Changes in pulmonary flow-resistance, elastic behaviour and ventilation were used as toxicological criteria rather than mortality and lung pathology.

An increase in resistance to air flow was produced by all the concentrations tested, in most concentrations this was accompanied by a significant decrease in compliance.

A toxic aerosol of particles large enough to be stopped in the upper respiratory tract may cause few symptoms even in fairly high concentrations. The 7 μ particles of sulphuric acid caused only slight increase in resistance in a concentration at which the smaller particles produced a very marked response. However, in high concentrations the 2·5 μ particles produced a greater response than the 0·8 μ particles.

There are many further details given of the effect of varying particle size and concentration. It appears that the 2·5 μ particles have their major effect at the level of the main bronchi, whereas the 0·8 particles are more likely to penetrate deep into the lung as would a gas.

Usually one response of the animal to an irritant aerosol is to produce an increase in respiratory work. This should be kept in mind if exercise is super-imposed upon exposure to sulphuric acid mist.

When subjected to large particle mists of sufficient concentration to produce death severe atelectasis and oedema of lungs resulted. This was interpreted as due

to plugging and closure of the main bronchi rather than due to a diffuse bronchial constriction.

T. O. Garland

NAKANISHI, S. & NAMIKI, S. **[Symptoms in Workers exposed to Isocyanates]** *J. Sci. of Labour.* Tokyo. 1958, Nov., v. 34, No. 11, 980–83. [In Japanese.]

The English summary appended to the paper is as follows:—

"There has been no report on the symptoms in workers exposed to isocyanates in Japan because isocyanates in industry have been introduced in this country in recent years.

"For the last two years the authors have made efforts in making investigation on symptoms in 54 workers who have been exposed to isocyanates for a period varying from one month to two years, eight hours daily. Nineteen out of 54 workers have presented some symptoms or complaints which are summarized as follows:

"The symptoms and complaints were seen with cough in 11 cases including 6 of spasmodic cough. Sore throat in 10 cases, increased sputum in 6 cases, rashes on the skin, gastro-intestinal disturbances, dyspnea, fatigue, appetite nausea, etc., were observed. It is noteworthy that there was a case of serious dyspnea which accompanied various critical symptoms."

HENSCHLER, D. Zur Frage der Gefährdung durch moderne Trikresylphosphate. **[Toxicity of Modern Tricresylphosphate]** *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1958, Nov., v. 8, No. 11, 265–7. [11 refs.]

In this paper the author discusses the toxicity of the older technical preparations of tricresylphosphate and points out that although the great toxicity of these was assumed to be due to the triorthocresyl constituent this view was erroneous for in his own published experiments he had found that the pure triorthocresyl ester was the least toxic of all the orthocresyl esters. The doses of the older and the newer tricresylphosphates which are toxic for man and animals are considered. Some experiments on chickens were carried out in which the animals were given varying doses of a modern tricresylphosphate preparation containing only 3·3% of *o*-cresyl instead of about 30% as in some of the older preparations. The doses were given on 6 days a week during a period of 2 months. From the results of the experiments, which are set out in a table and discussed, it is concluded that the danger to man of the modern preparations is slight in all but exceptional circumstances.

M. E. Delafield

BAKER, A. H., WHITNEY, G. F. H. & WORDEN, A. N. **The Toxic Hazard associated with Continuous-Flow Heat-Volatilized Insecticidal and Acaricidal Aerosols.** *Lab. Practice.* London. 1959, Jan., v. 8, No. 1, 3–10, 26, 2 figs. [13 refs.]

"Small mammals, birds and laboratory workers were exposed to the output of continuously operated pesticide vaporizers volatilizing aldrin or azoxybenzene or one of three dose levels of a mixture of lindane with D.D.T. Exposures lasted for periods varying between 178 and 386 days. The toxicity to house flies of residual deposits produced in the experimental rooms was tested and chemical analysis of affected animals was carried out. A direct relationship was found between dose level and insect response to surface deposits. Horizontal plates acquired a more effective deposit than vertical ones. Mouse fur was practically free from deposited lindane but the feathers of budgerigars readily accumulated a considerable amount. Output characteristics of the pesticides are discussed.

"Budgerigars were unable to survive at the highest dose of the lindane/D.D.T. mixture which had a mean value of 0·754 g.d.t. (g./day/1,000 cu. ft.). At the lower dose levels of the mixture (0·531 and 0·224 g.d.t.) and at doses of 0·500 g.d.t. of aldrin and 0·429 g.d.t. of azoxybenzene no deleterious effects were observed. In addition to the birds and mice other animals exposed to one or more of the treatments were: rats, dogs, guinea pigs, golden hamsters and human subjects; in no case did they suffer any detectable harm."

VANDEKAR, M. **The Toxic Properties of Demeton-Methyl ("Metasystox") and some Related Compounds.** *Brit. J. Indust. Med.* 1958, July, v. 15, No. 3, 158–67, 8 figs. [16 refs.]

The active ingredients in commercial demeton-methyl (Metasystox) are the 2 isomers, OO-dimethyl O-ethylthioethyl phosphorothionate (thionate isomer) and OO-dimethyl S-ethylthioethyl phosphorothiolate (thiolate isomer). By analogy with demeton (Systox) it seemed likely that the action of demeton-methyl would be due mainly to the sulphoxide and sulphone of the thiolate, produced metabolically both in plants and animals. The demeton-methyl isomers, however, also undergo other reactions in water and on storage, giving small yields of sulphoniuum compounds of very high intravenous toxicity.

The toxic properties of certain compounds may vary if they are allowed to age by storage or if they are estimated at different times after dilution in water. The author has studied these variations for commercial Metasystox and for the aged (converted) samples of demeton-methyl isomers and their derivatives, by carrying out acute (oral and intravenous doses) and chronic toxicity (feeding) tests on male and female albino rats. Chronic feeding experiments were performed on the rats given diets containing 50, 100 and 200 p.p.m. of the aged specimen of thiolate isomer or sulphoxide for 6 months. It would appear that such converted compounds may play the most important role in producing any toxic hazard that may arise from the consumption of the food treated with Metasystox. The experimental methods and the results are recorded in some detail in the paper.

The great increase in the toxicity of these materials either on storage or after dilution with water was clearly demonstrated by intravenous injections, whereas oral toxicity hardly revealed any change in toxicity. In all instances a comparison between aged and purified

compounds was made. The purified thionate isomer in large doses produced anaesthesia and haemorrhagic pulmonary oedema with no cholinergic symptoms, and the purified thiolate isomer produced a slight anaesthetic effect followed by cholinergic symptoms; the aged specimens of both thionate and thiolate isomers in very small doses produced cholinergic symptoms only. When sublethal single doses of the purified thiolate isomer or purified sulphoxide were injected intravenously prolonged symptoms were induced. The inhibitor was found to persist in the blood for several hours producing an almost complete irreversible inhibition of cholinesterase. The aged specimen of thiolate isomer produced symptoms of short duration and did not persist in the blood. Most of the inhibited erythrocyte cholinesterase recovered its activity rapidly and no significant inhibition of brain cholinesterase was produced. This effect of aging should obviously be borne in mind when chronic toxicity tests with purified (non-converted) specimens are planned.

In the chronic feeding experiments, brain and erythrocyte cholinesterase activities were strongly inhibited both with the thiolate isomer and sulphoxide; and the degree of inhibition corresponded to the levels fed in the diet. In spite of considerable depression of cholinesterase activity, no signs of poisoning by an anticholinesterase agent in the later stages of experiments were observed. At the highest levels there was some depression of growth in spite of an increased food intake. Scaliness of the tails developed towards the end of the experiment. Anticholinesterase activity of serum in rats after an experiment lasting for 6 months was moderately pronounced and essentially the same for both compounds. The original should be consulted for a lengthy discussion of the results and their significance.

P. J. R. Challen

HAYES, W. J., Jr., QUINBY, G. E., WALKER, K. C., ELLIOTT, J. W. & UPHOLT, W. M. **Storage of DDT and DDE in People with different Degrees of Exposure to DDT.** *Arch. Indust. Health.* Chicago. 1958, Nov., v. 18, No. 5, 398–406. [12 refs.]

Much is known about the storage of DDT and DDE in man, but there has been no systematic survey hitherto to determine whether groups differ in the amount stored in relation to exposure and occupation.

Autopsy samples of human fat were obtained from 10 people dying before the advent of DDT in the U.S.A. (1942). Analysis of these samples indicate that human fat does not contain any material which might be confused with DDT in the Schechter-Haller reaction.

Biopsy samples of fat were taken from a number of different groups; abstainers from meat (16), general population (61), those with significant environmental exposure (110), agricultural applicators of DDT within last 12 months (19) and applicators who have been thus employed but not within the last year (11).

Fat from those abstaining from meat held far less DDT than was found in the general population (2·3 p.p.m. as against 4·9 p.p.m.). There is strong evidence that fat of animal origin in the diet is the main source from which DDT and DDE is absorbed in those who have no particular occupational exposure.

People exposed at work to DDT stored only a little more than the general population, the amount being proportional to intensity and frequency of exposure.

There has been no progression in the storage of DDT in the general population since this was first noticed in 1950.

T. O. Garland

SHIRAKAWA, M. **Experimental Studies on the Toxicity of Benzene Hexachloride (BHC) and Dichlorodiphenyltrichloroethane (DDT). I. Toxicity Tests of the Insecticides following Various Administrations to Laboratory Animals.** *Kurume Med. J.* 1958, v. 5, No. 2, 65–86, 3 figs. [51 refs.]

The chemicals used in the experiments here described were the oil solutions of the pure crystals of gamma isomer of BHC, DDT and BHC mixture (50% gamma isomer and 50% other isomers) dissolved in several kinds of oils and fats making a concentration of 6% to 10%.

When these solutions were injected under the skin of rats and mice, the acute lethal dose of BHC and BHC mixture was about the same, the animals first showing an increased rate of respiration, then excessive activity with haemorrhages from nose, eyes and the vagina in females. Convulsions preceded death, which occurred after varying periods (from a few hours to 4 days in rats, 5 minutes to 3 days in mice).

The quantity of DDT required for a lethal dose was about twice the amount needed with BHC. The symptoms of DDT poisoning included tremors which were usually absent in the BHC cases. A number of animals that developed marked tremors nevertheless recovered completely.

When less than a lethal dose was given and then increased at weekly intervals little effect was found on the growth of the animals until the lethal dose was arrived at. When one-tenth to one-fifth of a lethal dose was given daily for 40 to 48 days growth was affected only with BHC mixture. When a daily dose of 100 mgm./kgm. of BHC was given subcutaneously, 6 of 7 young rats died after convulsions which followed 2 to 5 injections. With a similar dose of DDT only 1 of 6 rats died 4 days later, the other 5 showing no symptoms.

When the injections were given into the peritoneal cavity symptoms of intoxication from gamma BHC appeared sooner than after DDT. When the oil solutions were fed into the animals' stomachs through a catheter the lethal dose as before was associated with convulsions after gamma BHC and with severe tremors passing into paralysis after DDT. When the oil solutions were applied to shaven areas of skin on the back of the neck, gamma BHC was found again to be more toxic than DDT. However, the absorption of DDT by the skin route was quicker than of gamma BHC, the reverse of which was found when the oils were injected intraperitoneally.

None of these solutions used in ointments for over 300 human beings suffering from parasitic skin infections appeared to cause any toxic symptom.

T. O. Garland

J. Amer. Med. Ass. 1958, Nov. 8, v. 168, No. 10, 1351–9. [18 refs.] **Some Medicolegal Aspects of Occupational Dermatoses.** [Report prepared by the Committee on Occupational Dermatoses (Birmingham, D. J., Chairman) of the Council on Industrial Health, American Medical Association (Holland, B. D., Secretary).]

Everybody will agree that some sort of insurance must be made against the mishap to a workman who, whether or not through any fault of his own, becomes unable to pursue a remunerative or satisfying occupation or even to earn his living at work—and it is obvious that, to be effective, provision of this kind cannot be left to the initiative of the individual.

The object of most workmen's compensation legislation is to assure payment to the worker for wages lost and medical costs incurred because of illness acquired on the job and, if complete rehabilitation is not secured, to compensate him for his reduced industrial status. The compensation laws vary from one state of the U.S.A. to another, as also does the interpretation of the principles embodied in them.

This report is almost wholly composed of cases illustrating the difficulties of interpreting the intention of the law and the uncertainties which not only make unnecessary expense for the employer but lead to results which do not always appear fair to the workman.

Between the lines we read that the position has altered unpredictably since the principle of compensation was first established, to some extent by the principle itself which has been unconsciously exploited by the workman, ultimately to his own great disadvantage. The lack of any accepted ethical system hampers both dermatologists in giving opinions and the courts in making their decisions.

A satisfactory answer to one question, "What constitutes an occupational skin disease?", is here allowed to appear: any abnormality of the skin resulting from an accident sustained at work or from exposure to noxae encountered during the performance of that work. Is compensation to be awarded not only for disability but also for disfigurement or latent sensitization? Is aggravation of some pre-existent dermatosis to be considered only in regard to a temporary worsening terminating at the first remission; or can it be held responsible after the initial spell of incapacity, for the whole of the further course of the disease. Who, for instance, is to be responsible for aggravation resulting from diagnostic measures undertaken for the purposes of a decision of the court? In the case of allergic sensitization, or the establishment of a condition that relapses, or a chronic one subject to recrudescences, is the original or the present employer to be held responsible?

Who is to take care of the rehabilitation of the disabled worker?

All these problems, some of which have been partly solved in the U.K. by the National Insurance (Industrial Injuries) Act, are presented but clearly without hope of satisfactory solution. For it is evident that the main weakness of the arrangement here as in the U.K. stems from the attempt to differentiate between industrial injury and spontaneous disease, the difficulty of obtaining disinterested or useful advice in regard to future employment, and indeed the reluctance to accept it when it happens to be available which again inevitably stems from controversy in regard to responsibility.

J. H. Twiston Davies

Netherlands Society of Allergy [Organized by] in co-operation with the Netherlands Inst. for Preventive Med. & Netherlands Soc. of Occupational Med. under the auspices of the European Academy of Allergy. **Occupational Allergy. Lectures held during a Course on Occupational Allergy at the Hague in May, 1958.** pp. xvi + 329, numerous illustrations. 1958. Leiden: H.E. Stenfert Kroese N.V., P.O. Box 33, 38, Pieterskerkhof, Holland. [Fl.30.]

This handsome but not too ponderous volume comprises the text of 38 lectures given in an instructional course on occupational allergy at the Hague in May 1958. The reader receives the impression of a high incidence of allergic affections in industry and of a pretty widespread belief that atopy and an inherited predisposition to allergic reaction are important factors. Only W. B. Gerritsen questions if it is right to reject candidates for employment because of recurrent dermatitis, eczema and other itching dermatoses, but even he attributes polysensitivity (as manifested by the well known situation in which "every job becomes impossible") to resumption of work before healing of allergic dermatitis. P. H. Nexmand, however, concludes that occupational allergy is infrequent in Besnier's prurigo and that the real handicap in that syndrome is intolerance of environmental temperature-changes and sweating. [The reviewer would add that in his experience the type of personality commonly associated with Besnier is inconsistent with the quest for compensation.] J. W. H. Mali also reminds us of the existence of constitutional maladies and that the demand for relief may be a more important factor than causation in the relationship between housewifery and eczema of the hands.

D. A. Williams, who designates asthma, urticaria, eczema and dermatitis as allergic maladies, has tried his best to extract useful information from the statistics of the Ministry of National Insurance. This group of diseases, whatever we may choose to call it, accounts for about the same amount of incapacity as peptic ulcer. He indicates that, after coal miners, "workers in unskilled occupations" and "water, air and other workers in transport and communications" [which one supposes to include the Post Office], of the "occupations listed in order of increasing prevalence of spells of incapacity" railway workers lead the field. But he leaves us to guess why.

In general the contributors appear to have taken the complaints with which they have had to deal at their face value and the result is a long catalogue of industrial hazards, with detailed accounts of investigations by means of epicutaneous scratch and intradermal skin testing.

W. Burckhardt describes his alkali-neutralization and alkali-resistance tests. R. Voorhorst tells us how to prepare extracts, W. J. F. Van der Bijl and W. J. Quarles van Ufford how to demonstrate eosinophils in exudate, H. J. Ten Cate how to measure the vital capacity of the lungs before and after inhalation of an aerosol of the suspected allergen. J. W. H. Mali gives us some concise and valuable comments on patch testing. He also provides a delightful account, marred only by misprints and spelling mistakes, of the anatomy and physiology of the skin which by itself is well worth the price of the book. A. W. Frankland defines the uses of adrenaline, isoprenaline, steroids and antihistamines in the treatment of acute allergic mishaps. He recommends caution in the local treatment of conjunctiva, upper respiratory tract and in particular the skin by which he finds a simple lotion tolerated better than certain more enterprising remedies.

A. Nilzen discloses that in Sweden penicillin is still used therapeutically in dermatological practice and describes methods for detecting allergy and for desensitization. F. A. Nelemans considers that "in view of the variety of drugs available for all kinds of diseases, there is no great danger that the few people who become sensitized will run extra risks in case of illness". That is of course if one managed to avoid infection by treponemes. In a study of industrial disease in the pharmaceutical industry he did not discover much allergy though "the situation varies from firm to firm without one being able to explain the difference".

In the nursing profession, however, allergy to penicillin, streptomycin and chlorpromazine is rampant and, in France, where the basis of compensation for industrial disease is a system of limiting indices (that is to say if, for example, a lead worker develops any kind of nephrosis he would be considered to be suffering from lead nephritis irrespective of the history of any other signs, *e.g.* lithiasis) and the only dermatosis scheduled is that produced by streptomycin, chlorpromazine and nickel, and then only if verified by one or several positive skin tests: thus, according to C. Albahary, A. Cavigneaux and P. Bessede, contradicting the whole principle of presumption of origin ruling in respect of other industrial diseases.

Many contributors describe the allergic hazards in particular industries: F. F. Hellier in wool, K. E. Malten in dyeing, H. H. Schwarting in printing, J. Turiaf and J. Tabart, E. Sidi, R. Longueville and M. Hincky, and Quarles van Ufford in the medical and allied professions. Some discuss important irritants in detail while others deal with the various organs and systems involved. R. Surinyach expresses the need for closer cooperation between allergology and industrial medicine and, in his opening address Werner Jadassohn happily defines these two disciplines as branches of medicine intersecting at right angles the traditional regional specialties. In a foreword, D. A. Williams defines the purpose of the enterprise, of which this book constitutes the record, as a welding together of the views of European workers on occupational allergy. A great mass of information has certainly been exchanged but the reader may well deem it fortunate that unanimity does not result. *J. H. Twiston Davies*

Madhekar, I. K. **Some Aspects of Toxic Hazards in Penicillin Manufacture.** *Hindustan Antibiotics Bull.* 1958, Nov., v. 1, No. 2, 63–7.

This is a short paper in which some account is given of the possible industrial hazards of the chemicals used in the manufacture of penicillin. Penicillin itself is relatively harmless although some allergic reactions and melanoglossia may develop in some workers. A few particulars are given of the symptoms and pathological effects which may result from exposure to the solvents acetone, amyl acetate, butyl acetate, n-butyl alcohol and iso-propyl alcohol. Short reference is made also to the possible dangers or harmlessness of the acids, alkalies, alkaline salts, antifoams, various chemical disinfectants, ultra-violet light and ozone produced in the vicinity of ultra-violet lamps to which workers in the manufacture of penicillin may be exposed. A short list of the "remedial measures for preventing toxic hazards in Hindustan Antibiotics" is given. *M. E. Delafield*

Morris, G. E. **"Chrome" Dermatitis. A Study of the Chemistry of Shoe Leather with particular reference to Basic Chromic Sulfate.** *Arch. Dermat.* 1958, Nov., v. 78, No. 5, 612–18. [18 refs.]

The particular form of chrome, the trivalent basic sulphate, which is employed in tanning has long been supposed to be non-allergenic; and in most studies of dermatitis of the feet attributed to shoes the emphasis has been on dyes, resins or rubber adhesives. Most of us, it is true, will have patch-tested in such cases with the hexavalent $K_2Cr_2O_7$ and perhaps also with other salts of chrome, regardless of the fact that they are not used in tannery and unlikely to be found in shoes.

Though he gives an exhaustive list of skin hazards in the leather industry the author regards chrome dermatitis as the main one and states that basic chrome sulphate is known to be the cause of it. Now that we know that the basic sulphate can be leached out of leather by the lactic acid in sweat many mysteries of foot dermatitis should be solved by patch-testing with the appropriate salt.

Although this paper primarily concerns the consumer end of the leather trade there is some description of processes and of 2 cases of dermatitis produced by 3-valent chrome in leather workers [though it does not state that they were not also allergic to 6-valent salts]. *J. H. Twiston Davies*

Long, P. I., Jr. **Subungual Hemorrhage in Pan Washers. Preliminary Report.** *J. Amer. Med. Ass.* 1958, Nov. 1, v. 168, No. 9, 1226–7, 2 figs.

A lesion of the nail-bed, new, bizarre and unexplained by circumstantial study in the light of existing dermatological knowledge, occurred in 3 out of an unspecified number of men employed at washing dishes in the kitchens of a veterans' hospital. The only difference between the work of the victims and that of the unaffected workers seems to have been that the victims wore heavy rubber gloves. The patients were not demonstrably allergic to the rubber and it is

thought that some modification, by reaction with gloves, sweat or keratin, of the detergent might possibly be responsible. But it happened that the detergent was changed between the occurrence of the first case and the other two.

The lesion consisted of multiple irregular haemorrhages into the nail-bed which in all cases ceased to appear when the men left the job. In one case a hole had to be drilled in the nail to relieve pain. Severe damage to the nail-bed is clearly possible.

In view of the banal character of the hazard the author abstains from any facile attribution to trauma and maceration. [The condition seems to the reviewer to fall into that class of happenings so often reported in industry in which a hazard endured uneventfully by large numbers seems to produce at one particular place and time a small crop of cases of a kind neither seen before nor heard of again.] *J. H. Twiston Davies*

PRACTITIONER. 1958, Nov., v. 181, No. 1085, 553–602, 4 figs. [Numerous refs.] **Radiation Hazards.**

1. *The effects of radiation on the individual* by J. F. LOUTIT, pp. 553–558. What the author is mainly concerned with is the sequelae after small doses of high intensity radiation such as diagnostic X-rays at infrequent intervals or a chronic exposure of the whole body to radiation at a low dose-rate; the latter conditions arise in work with radio-active materials and in enhanced background radiation conditions. Leukaemia of most sorts, except chronic lymphatic, has appeared in 3 categories: (1) radiologists, (2) cases of ankylosing spondylitis treated by radiotherapy in which most of the active bone marrow in the bones of the trunk have received substantial doses intermittently at a high dose-rate, (3) survivors at Hiroshima who received in one flash a large gamma ray dose to the whole body.

2. *The genetic hazards of radiation* by Alan C. STEVENSON, pp. 559–571. On the subject of radiation-induced mutations the author thinks that we can afford to ignore gross chromosomal damage as compared with point mutation damage from radiation. The essential change induced at a locus is a single molecular rearrangement and this can be effected by a single tract of radiation, hence there is no threshold dose of radiation for a mutation to occur; this is a concept of extreme importance in radiation genetics. It has been variously estimated that there are between 5,000 and 50,000 gene loci on human chromosomes and the author has for convenience in discussion put these into 5 classes; the assignment of genes amid these classes can best be appreciated by one completely conversant with the subject. In accord with other writers, the author is convinced that radiation-induced mutations are only harmful to man.

3. *Radiation from natural sources* by F. W. SPIERS, pp. 572–575. The author cites the various sources of radiation to which we are subjected; these are external to us or within our bodies, part of our make up in fact, varying with locality to some extent. A representative value for the average dose inevitably received by human gonads in Britain is given by the author as 100 mr. per year, 28 mr. by cosmic rays, 20 mr. by body potassium, 48 mr. by gamma rays and the remaining 4 mr. by radium or thorium in the body. Bone contains less potassium than the soft tissues but more radium and thorium deposited therein by food and water.

4. *The hazards of diagnostic X-rays* by W. M. C. BROWN, pp. 576–581. The author gives in tabular form the gonad doses per radio-diagnostic examination for 13 different sites of enquiry; there is a very big range as might be anticipated, pelvimetry of the male involves no dose to the gonads, while for females this and pyelography account for the largest doses. The author is, however, mainly concerned here with the possible induction of leukaemia by means of X-rays; he has postulated that leukaemia may be the outcome of a simple mutation in a somatic cell. He admits that this is still a controversial matter.

5. *Strontium^{90} and human food* by R. S. RUSSELL, pp. 582–588. After any fallout ^{90}Sr will settle on the foliage, on stems of plants and on the soil. Cattle grazing over such terrain will ingest some of this dangerous material which, making its way into the milk, will provide another risk for milk drinkers, the chief of these being children. The author gives a good description of how ^{90}Sr and Ca get distributed to the roots of plants and become disseminated throughout the soil. A careful watch is evidently being taken on the unwanted appearances of this dangerous radio-active isotope.

6. *Radiation hazards and public health preventive measures* by A. B. SEMPLE, pp. 589–593. The author gives a brief account of present-day radiation hazards, especially those of contamination by radio-activity in the atmosphere or water supplies. He insists that a wide dissemination of the fundamental principles of nuclear energy is essential among those concerned with the public health. He suggests further that every County Council and County Borough Council should maintain an efficient monitoring service to deal with these contaminants promptly.

7. *The control of radiation hazards in industry* by A. S. MCLEAN, pp. 594–597. Emphasis is laid by the author on the fact that the medical officer finds himself engaged in the practice of preventive medicine *par excellence*. Once radiation injury has occurred, unless of a transient nature, it often proves rather untractable. The author holds the view that "although a number of substances have definite protective properties when administered before radiation exposure occurs, none is effective after the event". This opinion is singularly at variance with those in the concluding article of this symposium, No. 8.

8. *Civil Defence and atomic warfare* by E. R. CARLING and G. R. STANBURY, pp. 598–602. This article begins thus:—"'Suppose ten million killed. There remain forty million to be cared for.' Major-General S. F. IRWIN". And it continues thus:—"A surprise or unresisted attack by a fleet of bombers carrying thermo-nuclear weapons could paralyse this Island and put it out of action. . . . The effect would be produced partly by material destruction, partly by elimination of stored, imported or growing food supplies and partly by biological damage from ionizing radiation."

The paper is concerned solely with the last factor.

In the event indeed it would be largely a question of succouring those at the periphery. There has been no defeatist attitude in Britain for we read "Notwithstanding the appalling difficulty every Authority has faced up to the situation. . . ." *S. Russ*

LIEBEN, J. **Shoe-Fitting Fluoroscopes—their Outlawing in Pennsylvania.** *Amer. Indust. Hyg. Ass. J.* 1958, Oct., v. 19, No. 5, 382–3.

"Shoe-fitting fluoroscopes are devices which cause a relatively high radiation exposure to the feet of the unsuspecting customer. They were most often operated by untrained personnel and it was felt that they constituted a source of unnecessary radiation exposure which could not be justified and could not operate in compliance with the maximum permissible doses as outlined in *Pennsylvania Regulation 433 'Radiation Protection'*. For that reason they were outlawed in Pennsylvania in February 1957."

Atmospheric Pollution

CAREY, G. C. R., PHAIR, J. J., SHEPHARD, R. J. & THOMSON, M. L. **The Effects of Air Pollution on Human Health.** *Amer. Indust. Hyg. Ass. J.* 1958, Oct., v. 19, No. 5, 363–70, 7 figs. [16 refs.]

In 1955–6 3 pilot studies of the epidemiological effects of air pollution were made in Cincinnati. This paper describes the third of these, which lasted from October to December 1956, and gives some preliminary results.

3 types of observation were made: (1) "Complaints" (subjective observations) were recorded by patients; (2) "Reactions" (objective observations) were measured thrice weekly by maximum inspiratory and expiratory pressures, timed vital capacities and carbon monoxide diffusion; and (3) environment was assessed by hourly measurements of smoke, temperature and humidity outdoors and in the homes of patients, and by gaseous acid outdoors in all surveys and indoors as well in the third. The indoor temperature was normally 70–80°F.

A very large number of observations were collected, but they appear to refer to 10 patients only. The results obtained are outlined and discussed qualitatively.

J. McK. Ellison

LUPU, N. & VELIKAN, K. [**Pneumoconiosis in Children of Industrial Towns where the Atmospheric Air is polluted with Dust containing Silicon Dioxide**] *Gigiena i Sanitariya.* Moscow. 1958, v. 23, No. 12, 10–13, 4 figs. on 2 pls. [In Russian.]

The English summary appended to the paper is as follows:—

"The authors have made clinical and roentgenological examinations of 800 school children, 10–15 years old, who have been born and lived in the districts of 4 industrial towns with heavily polluted air. A considerable percentage of children had a mild form of diffuse sclerosis of lungs. The children from the control groups, living in the cleanest districts of the same towns, did not have any lesions of the lungs."

The table included in this text gives the following figures:—

"Results of a roentgenological examination of the child population (percentage of children in whom changes were discovered)"

Character of change	Town No. 1		Town No. 2		Town No. 3		Town No. 4	
	polluted area	control area	polluted area	control area	polluted area	control area	polluted area	control area
Diffused sclerosis	4	0	3	0	15	0	0	0
Other changes in the pleura and lungs	15	5	29	22	30	17	44	12
Normal lung picture	81	95	68	78	55	83	56	88

Physiology as Applied to Hygiene

STARLINGER, H. Die tageszeitlichen Schwankungen in der Elektrolyt- und 17–21-Dihydroxy-20-Ketosteroid-Ausscheidung im Harn und ihre Änderungen durch verschiedene Arbeits- und Klimabedingungen. **[Daily Fluctuation in the Urinary Excretion of Electrolytes and 17–21-Dihydroxy-20-Ketosteroids and its Modification by Different Working and Climatic Conditions]** *Internat. Ztschr. f. Angewandte Physiol.* 1958, v. 17, No. 4, 341–70, 11 figs. [33 refs.]

In this long paper there is first a discussion of much of the literature on the urinary excretion of electrolytes and steroids to introduce a detailed description of the experimental work carried out by the author. The experiments were conducted on 2 healthy men who were kept in an experimental room in which the temperature could be varied and where measured amounts of work were carried out. Samples of urine voided in the night before the beginning of the experimental day and at 7 different points in the course of the day were analysed for their content of sodium, potassium, phosphorus, chloride and ketosteroids by methods which are described. In a series of analyses of the blood the electrolyte concentration was determined but not the ketosteroid content. The extensive analytical data obtained are set out in a series of numerical tables and are fully described and discussed. Among the main results of the experiments it was found that work and particularly work in a hot atmosphere results in an increase in the potassium concentration but a marked diminution in the sodium concentration in the urine whereas the chloride concentration remains practically unchanged. Hence the ratio of potassium to sodium excretion is greatly increased. It was not possible to recognize any simple relationship between the urinary excretion of sodium and potassium and that of the ketosteroid. *M. E. Delafield*

Hygiene of Buildings

HEAT REGULATION, VENTILATION AND LIGHTING

BEDFORD, T. **Research on Heating and Ventilation in relation to Human Comfort.** *Heating, Piping & Air Conditioning.* 1958, Dec., v. 30, No. 12, 127–34, 4 figs. [36 refs.]

In this paper Dr. Bedford reviews the work carried out by his associates and himself over a number of years on the effect of the thermal environment on human comfort, efficiency and general well-being. This work is considered under the following headings: thermal measurements, indices of warmth, comfort zones, skin temperature and comfort, pleasant environments, ceiling and floor heating.

It is well known that the kata thermometer and hot wire anemometer are not reliable instruments for the measurement of low air speeds and reference is made to the ionization anemometer which is considered to be more accurate. The measurement of the Mean Radiant Temperature (MRT) is discussed and we are reminded that in an occupied room the MRT is affected by the presence of occupants and may be increased by as much as 4°F. or more in crowded assemblies. Various indices of warmth have been devised, and these indices have been compared by the author in a study of the comfort of people performing light industrial operations in British factories during the heating season, the highest correlation of comfort votes with indices of warmth occurring with those which made allowances for radiation. Following on this and other observations the author has advocated that in the determination of the effective temperature the globe temperature be substituted for the dry bulb temperature. The effective temperature thus simply adjusted being known as the "corrected effective temperature".

In his observations on the comfort zones the author states that there are wide divergences between the thermal comfort zones that have been determined for various places and seasons. Examples of these are given in the text. It is recommended that the thermal comfort zone should be defined as the range of temperature within which 86% of the comfort votes recorded range from comfortably cool to comfortably warm. Skin temperature has often been used to assess thermal comfort but the fact that individual variations of temperature are great would seem to make skin temperature of dubious value as an index of comfort even though it may give interesting physiological information.

Dr. Bedford points out that the maintenance of the desired effective temperature does not necessarily ensure that the environment will be a pleasant one. One must also take into consideration the distribution of heat, the adequacy and variability of air movement, and the variability of the temperature with particular reference to temperature gradients which may occur between floor and ceiling. The humidity should not be greater than 60% and very low humidities should also be avoided.

In a room heated by ceiling panels the elevation of the MRT due to the panels should not exceed 4°F. When floor heating is used the surface temperature of the floor must not be excessive; according to recent experiments it should not be above 77°F.

J. R. Brown

Sanitation

WATER AND SWIMMING BATHS

(Including the bacteriology of water supplies)

HABS, H. & LANGELOH, Hanna. Die Bedeutung der sogenannten atypischen Colibakterien für die Trinkwasserbeurteilung. [**The Significance of the So-Called Atypical Coliform Bacteria in the Examination of Water**] *Arch. f. Hyg. u. Bakt.* 1958, Sept., v. 142, No. 6, 401–14, 1 fig.

The authors compared the number of typical and atypical *Escherichia coli* in 6,506 samples of water collected from the area controlled by the Hygiene Institute of Heidelberg. A total of 2,206 coliform strains were isolated and, of these, 68% were typical *E. coli*; of the atypical *coli* strains present, 62% belonged to the type *E.* [*Citrobacter*] *freundii*.

A comparison between the general colony count and the coliform and coli contents was made and a statistical correlation was found.

Samples of water from sandstone wells which only rarely showed an increase in the colony count sometimes showed atypical *E. coli* which heralded the appearance of typical *E. coli* after heavy rain. The bacteriological results were in accordance with what might have been expected from the topographical situation. The authors conclude that the presence of atypical *E. coli* is not so much an indication of faecal contamination but serves as ground for objection to the water because of the knowledge which this bacterium implies, namely, that insufficiently filtered surface water has gained access to the source. *E. Windle Taylor*

GUTHOF, O. & DAMMANN, G. Uber die Brauchbarkeit von Enterokokken-Testen zur Beurteilung von Trinkwasser und Oberflächenwasser. [**The Value of the Enterococcus Test in the Examination of Drinking and Surface Waters**] *Arch. f. Hyg. u. Bakt.* 1958, Oct., v. 142, No. 7, 559–68. [29 refs.]

Tests for enterococci constitute a worthwhile addition to the bacteriological examination of water.

In the selection of suitable media the sodium azide content and the *p*H are of decisive importance. In an acid medium sodium azide is a poor selective agent, but a good one under alkaline conditions. The selective action in alkaline conditions can be made still better by a higher sodium chloride concentration. Enterococci are not damaged at a *p*H of 8·3 in sodium-azide-sodium-chloride medium whereas *Escherichia* and coliform bacteria are completely eliminated and spore-bearers largely suppressed.

False positive results in 1-stage procedures were found to be mostly due to an enterococcus-like air organism, the diplococcus I. Plating out can be done by incubating at 45°C. on crystal violet or ethyl violet confirmatory medium, or by the differentiating action of a selenite plate.

A 2-stage method for the cultivation of enterococci is described. First a primary culture is made on dextrose broth at *p*H 8·3 containing 0·03% sodium azide and 3% sodium chloride and this is followed by subculture on a selenite plate. The authors conclude that the enterococcus test is easy to perform and of particular value in assessing the significance of coliform counts. They recommend its adoption as a worthwhile addition to the routine bacteriological examination of water samples.

100 water samples from springs with varying *coli* counts were investigated simultaneously for *Escherichia* and enterococci. A close agreement is shown in the results. Also in 80 samples of Rhine water taken on different days and from different places approximately similar enterococci and *coli* titres were found.

E. Windle Taylor

SPITZ, Grace C. S., TAYLOR, F. B. & HARRIS, W. L. **Experience in maintaining Constant Fluoride Concentrations.** *Amer. J. Pub. Health.* 1958, Dec., v. 48, No. 12, 1651–9, 4 figs.

TAYLOR, Edwin Windle [M.A., M.D., B.Ch., M.R.C.S., L.R.C.P., D.P.H.] [Revised by]. **The Examination of Waters and Water Supplies** [THRESH, BEALE & SUCKLING]. 7th Edition, pp. viii + 841, 51 illustrations. 1958. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [£5.]

This book was reviewed on p. 182.

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

GAMESON, A. L. H. & WHEATLAND, A. B. **The Ultimate Oxygen Demand and Course of Oxidation of Sewage Effluents.** *J. & Proc. Inst. Sewage Purification.* 1958, Pt. 2, 106–17, 7 figs. [16 refs.] Discussion 117–19.

The authors express the opinion that the 5-day 20°C. BOD is unsatisfactory for assessment of the polluting effects of a sewage effluent on a river, because:

1. Some rivers, especially tidal estuaries, continue to be affected by dissolved oxygen depletion, even after dilution for 5 days.
2. The BOD does not include nitrification normally, but this may start immediately in a river, owing to the presence of nitrifiers.
3. A large amount of the suspended matter in the effluent may settle out fairly quickly, to give mud deposits which are subsequently oxidized.

By means of a respirometer, the ultimate oxygen demand (UOD) of various sewage effluents was determined. The unsuitability of the BOD was further demonstrated by the fact that the ratio of BOD to UOD was variable, depending on the time lapse between

determination of the BOD and the taking of the sample. This, of course, follows from the stepwise character of the oxidation of first, carbonaceous material and then nitrogenous matter.

By assuming a respiratory quotient of 1 for sewage the authors calculate that the UOD may be represented by the formula UOD = 2·67 (organic carbon) + 4·57 (ammoniacal nitrogen + organic nitrogen).

This calculated value of UOD was shown to agree closely with experimental values on sewages from all stages of treatment.

The relation between the UOD/BOD ratio and the N/C ratio was shown to deviate from the linear relationship calculated by assuming the pseudomonomolecular equation for first-stage BOD oxidation. This deviation led the authors to suspect the validity of applying first-order kinetics to the first stage of the BOD curve. The equation was modified in 3 ways:

1. by application of the retarded exponential,
2. by application of the composite exponential,
3. by the application of ORFORD'S logarithmic-time equation.

These curves were shown to fit experimental results very closely. The use of the composite exponential equation shows up very well the way that the different components of a sewage are broken down at varying rates. The authors' use of this type of equation to trace the way in which compounds of varying resistance to biological oxidation are removed during sewage treatment is excellent.

The UOD, it is concluded, is good for comparing sewage effluents, and for testing the actual effects of a sewage effluent on a river. It is recommended that as an adjunct to the BOD test, determinations of organic carbon and organic nitrogen be carried out, especially in experimental work.

The discussion which followed brought out a most interesting comparison of the authors' formula for the calculation of UOD and the McGowan formula for the determination of the strength of sewages.

UOD	= 2·67 × organic carbon	+ 4·57 × oxidizable nitrogen
McGowan strength for settled sewages.	= 6·0 × $\frac{N}{8}$ PV	+ 4·5 × total nitrogen

The relation between N/8 PV [permanganate value] and organic carbon was found to average about 1 to 2·0. Thus the UOD formula can be expressed as 5·3 × N/8 PV + 4·57 oxidizable nitrogen—a form most similar to the McGowan strength formula.

D. Jenkins

DOWNING, A. L. & SCRAGG, L. J. **The Effect of Synthetic Detergents on the Rate of Aeration in Diffused-Air Activated Sludge Plants.** *Water & Waste Treatment J.* London. 1958, Sept.–Oct., v. 7, No. 3, 102–7, 8 figs. [14 refs.]

The performance of a laboratory model of a continuous diffused-air activated sludge plant, treating synthetic sewage, was studied both in the presence and absence of anionic synthetic detergents.

The aeration vessel consisted of a Pyrex cylinder, 15 ft. long and 3 inches in internal diameter, with a capacity of 19·5 litres. Mixed liquor, containing about 3,000 p.p.m. suspended solids, was aerated for about 8 hours and settled for about 2 hours.

The equilibrium values for the concentration of dissolved oxygen in the mixed liquor were calculated and an equation for the calculation of the absorption coefficient of oxygen, (k), was derived.

The performance of the plant was assessed by estimations of ammonia, organic carbon, total oxidized nitrogen, suspended solids and the detergent (by the method of LONGWELL and MANIECE, *Analyst*, 1955, v. 80, 167) in the effluent, and of ammonia and organic carbon in the influent. The oxygen contents of the incoming and outgoing air streams was recorded continuously. Dissolved oxygen in the mixed liquor was determined by the copper sulphate-sulphamic-acid inhibitor modification of the Winkler method.

The authors were led to believe that the inhibitor was not completely effective, as dissolved oxygen values below those expected were obtained with determinations on the mixed liquor; the discrepancy was reduced by centrifuging and was lower with liquors containing low concentrations of suspended solids. The authors believe that, below concentrations of about 2 p.p.m. of dissolved oxygen, the method was accurate to within 0·2 p.p.m.

2 series of experiments were carried out. When there was an adequate supply of oxygen, 10 p.p.m. of detergent reduced the value of k by over one-third of its value for detergent-free sewage, but in spite of this, no detectable deterioration in the quality of the effluent was noticed.

When the oxygen supply was limited, so that no nitrification occurred in detergent-free sewage, addition of 10 p.p.m. of detergent caused a drop of almost two-thirds in the value of k. When detergents were excluded from the sewage k reached a value of 21% below that of its original value.

The amount of ammonia oxidized dropped from 60% to 10% and there was a 60% increase in the organic carbon content of the effluent. The performance of the plant could be restored to normal by trebling the air supply or omitting the detergent.

The authors were led to suspect that the rate of oxygen utilization by the activated sludge decreased at low values of dissolved oxygen (below about 0·3 p.p.m.).

The reduction in the potential maximum oxygen demand was shown to correlate closely to the estimated drop in the capacity for oxygen absorption in the presence of synthetic detergents. However, a 65% reduction in k produced only a 30% reduction in purifying capacity.

It seems that a reduction of k of about 54% occurred with single orifice and conventional type diffusers, while with block diffusers similar to the type used in the experimental work a reduction in k of about 65% was observed.

2 peculiar effects were noticed—the tendency for the value of k in detergent-free mixed liquor to decrease gradually with time, and the apparent sudden change in the performance of a sintered diffuser.

[The reviewer feels that the value of the paper would have been enhanced if the figures could have been printed larger and clearer.] *D. Jenkins*

TRUESDALE, G. A. **Foaming of Liquids containing Synthetic Detergents.** *Water & Waste Tratment J.* London. 1958, Sept.–Oct., v. 7, No. 3, 108–11, 4 figs.

A study has been made at the Water Pollution Research Laboratory, Stevenage, Hertfordshire, of the relation between foaming, the type of liquid and the type and concentration of detergent present; from this study a routine method for the rapid testing of samples has been evolved.

The apparatus used consisted of a 6 ft. vertical glass pipe of 4 inches internal diameter, fitted with a 1 inch cube diffuser and a sampling tap at the lower end. Air was blown through a 3 ft. column of liquid under a pressure of 4 lb. per sq. in. at a rate of 90 ml./minute. Foam height was measured at intervals. No strict control of temperature seems to have been made—"experiments were made at about 15°C.".

Experiments were carried out on detergent-free synthetic sewage, tap water, filter effluent and settled sewage. A mixture containing equal weights of 7 proprietary household detergents was tested in the above liquids at concentrations between 0·5–20 p.p.m. as Manoxol O.T. (detergent concentrations as Manoxol O.T. determined by the LONGWELL and MANIECE method).

Typical experiments showed a linear increase in foam height with time, to a maximum value. The maximum height of foam and the time taken to achieve it increased with detergent concentration. The tendency to foam was greatest in tap water and became progressively less as the pollution was increased, however the proportion of detergent lost from a particular type of liquid in the production of a foam was constant for that liquid and independent of the detergent concentration.

These experiments also show that the amount of detergent present in a given volume of foam was a reasonably constant figure. The author has suggested that the constancy of this figure may be related to the amount of detergent required to form a monomolecular layer at the air-water interface. By a rough estimation he has calculated the area occupied by 1 detergent molecule to be 135 sq. Å for Manoxol and 86 sq. Å for Teepol (a secondary alkyl sulphate). These figures are of the right order. Foam production thus would be dependent on the availability of sufficient detergent in the liquid; the presence of suspended solids which may adsorb detergents may account for the retention of some detergent and thus a reduction in foaming.

The routine test for the examination of the foaming tendencies of liquids measured the maximum height of foam that was produced in 8 minutes with a flow rate of 90 ml./minute at a pressure of 4 lb. per sq. in. In its present form the test is suitable for comparison of the foaming properties of sewage and sewage effluent containing 0–8 p.p.m. of surface-active material as Manoxol O.T. *D. Jenkins*

Food and Nutrition

FOODSTUFFS

Composition and Bacteriological Control

ROYAL SOC. PROMOTION HEALTH J. 1958, Nov.–Dec., v. 78, No. 6, 711–31. **Symposium on the Food Hygiene Regulations with special reference to Food Poisoning** [GILLESPIE, E. H.; ROSS, A. I.; WADE, A.].

These 3 papers, which comprise a symposium on the Food Hygiene Regulations, 1955, were presented at a Sessional Meeting of the Royal Society for the Promotion of Health held at Chesterfield in June, 1958. There was a good discussion in which a speaker said, "There were many imperfections in the Regulations, as in all others, but, as all the speakers had agreed, the intentions for good transcended the imperfections".

In the first paper Dr. E. H. Gillespie summarized our present knowledge of the bacteria which are liable to cause food poisoning, of the infection and of the toxin type, their mode of spread, their source and the investigation of outbreaks. He pointed out several important points and defects in the Regulations concerning persons engaged in the handling of food (Part III), the temperature at which certain foods shall be kept (Part IV, para. 15), and the control of the transport of meat (Part VI, para. 29). Mention was also made of infection in fertilizers and artificial feeding stuffs.

In the second paper Dr. A. I. Ross described and set out in tables published statistics on the incidence, vehicles of infection and presumed causal agents of food poisoning in England and Wales. He gave his views on imperfections in the Regulations in respect of the washing of hands by food handlers, condition of equipment before use, adequate cooking, cooling of food and temperature control of gelatine in the manufacture of meat products. Experience of the operation of the Regulations in Leicester was also described.

In the third paper Mr. Alfred Wade discussed the Regulations from his experience as Chief Public Health Inspector, City of Nottingham. His criticisms and discussion of the Regulations related particularly to the requirements for the conduct of food handlers, the sanitary accommodation in premises, food stalls and the transport of meat. *M. E. Delafield*

MAIR, L. **Food Hygiene in the Open Air.** *Sanitarian.* London. 1958, Nov., v. 67, No. 2, 64–76, 8 figs. Discussion 76–80.

This paper was presented by Mr. L. Mair (Chief Public Health Inspector, City and County of Newcastle-upon-Tyne) at the Annual Conference of the Association of Public Health Inspectors held at Blackpool in September 1958. Some general considerations of the administration of "the contentious Food Hygiene Regulations, 1955" which "is more or less settling down on a reasonably comfortable bed of compromise" introduced a review of the present condition of the outdoor food trade. It is estimated that at present there are some 4,000 mobile food shops selling groceries, 1,000 selling fruit and vegetables and about 2,000 which retail meat. An increasing proportion of these shops are of entirely satisfactory design and equipment, but the hygienic problems which remain are those discovered in connexion with the open market, the street stall-holder, the fairground food vendor and the "ubiquitous barrow boy". The sections of the paper which followed contained able descriptions and discussions of (1) legal considerations, (2) food and drink hygiene at fairs, shows, race meetings and other outdoor events, in which there is a long account of the organization of the annual Temperance Festival held on a fairground in the speaker's district which is visited by about 1 million people during the week, (3) markets and (4) mobile street traders. To illustrate this last section there are some photographs of the interior of certain modern mobile shops.

This interesting paper was followed by an active discussion which was both valuable and humorous.

M. E. Delafield

COOKE, W. E. **Slaughterhouses.** *Sanitarian.* London. 1958, Nov., v. 67, No. 2, 81–94, 8 figs. [11 refs.] Discussion 94–8.

This paper was presented by Mr. W. E. Cooke (Chief Public Health Inspector, Bingley Urban District Council) at the Annual Conference of the Association of Public Health Inspectors held at Blackpool in September 1958. It is a study, based on much reading and consultation, which sets out to record the present position as regards slaughterhouses and meat inspection in England and Wales. "As a result of this study it is difficult to avoid the conclusion that the conditions under which meat is produced at present in England and Wales are on a lower standard than obtains in Scotland and many Western European countries."

There is a short but interesting account of some features of meat production in other countries with a particular description and plan of the Lausanne abattoirs. A section of the paper deals with the present position as regards slaughterhouses in England and Wales where there are 4,200 privately owned licensed abattoirs. New trends in slaughterhouse construction and working are discussed in the light of the recommendations of the Interdepartmental Committee on Slaughterhouses, 1955. The need for compulsory meat inspection is stressed, for "there is no law in this country to compel local authorities to inspect all meat prior to its sale for human consumption". Slaughterhouse improvement is discussed with a description, plans and photographs of 2 small modernized abattoirs, provided by the local authorities of Skipton and of Colne. The provisions of the Slaughterhouses Act, 1958, and the Draft Regulations are described and discussed in some detail. In the conclusion to the paper it is regretted that the subject of meat production has become such a political issue in the last 4 years, and furthermore, that although the Government hopes that the new legislation will bring about the desired "moderate concentration" of slaughterhouses within a few years, most public health inspectors are sceptical of this view. Some suggestions for securing future improvement are set out in detail. An active discussion followed the presentation of the paper.

M. E. Delafield

WILLIAMS, H. A. **Lead and Arsenic Poisoning with special reference to the Toxicity of Lead Arsenate Spray Residues.** *Roy. Soc. Promotion Health J.* 1958, Nov.–Dec., v. 78, No. 6, 732–40. [40 refs.]

For more than 50 years the possibility of injury to health from imported apples contaminated by lead arsenate has "exercised the vigilance of public health inspectors, and occasionally consignments of fruit bearing excessive residues have been detected". Attention was focussed on the possibility of lead and arsenic poisoning by the importation to the principal ports of England in January to March 1958 of £100,000 worth of apples from the Lebanon, most of which were grossly contaminated. The difficulties of satisfactory sampling of consignments of apples, each of which contains, say, 20,000 boxes of fruit, are described, but at the Port of London analyses of 64 samples from 3 consignments (varieties of apple were Golden Delicious and Red Starking) showed an average lead content of 10 parts per million with a range of 0 to 31 and an average arsenic content of 3·5 parts per million with a range of 0 to 16, calculated on the whole fruit. A study to determine the distribution of lead and arsenic in the fruit was undertaken and showed that only 25% of the total residue was contained in the peel around the stalk and the calyx and in the core, about 75% was in the remainder of the peel and less than 1% in the peeled flesh. Other sections of this article describe and discuss, with reference to the literature, the composition of the lead arsenate spray, the solubility of lead arsenate in the human digestive system, the toxicity of lead in man and animals, lead poisoning in children, the proposed limits for lead in food and the toxicity of arsenic. A final section on removal of spray residues states that a process of immersion of the apples in a 1% solution of hydrochloric acid containing a wetting agent, followed by washing with running water, has been published and appears to be effective and commercially practicable.

It is understood that appropriate measures are being taken by the Lebanese authorities to avoid further trouble of this kind, which it is believed was due to spraying too near to harvesting, lack of rain after spraying, the absence of testing and washing facilities and other factors.

M. E. Delafield

MARINI, E. & GALLASSO, A. Sul controllo sierologico delle carni costituenti le mortadelle. [**On the Serological Control of Meats Used in Sausages**] *Ann. d. San. Pubblica.* Rome. 1958, July–Aug., v. 19, No. 4, 801–7. English summary (3 lines).

Control of the nature of meats used in sausages depends on a precipitin reaction, with an extract from the meat itself and homologous antisera. While this is useful for sausages consisting of uncooked meat, it is, contrary to what is claimed, not practicable for meats in which cooking has denatured the specific proteins. In *mortadella* (or Bologna sausage) the temperature and method by which the meat is cooked are such that there is no complete denaturation of proteins and the precipitin reaction can still be regularly obtained. *Mortadella* normally consists of 70% lean meat, 20% fat, 2–4% skimmed milk, 2·5% sodium chloride and other chemicals: these are first kept at 60°C. for 9 hours, the temperature being then raised to 80°C. and maintained for 5 hours.

Extraction is carried out on a relatively large amount of sample, with 50 gm. of lean meat. This is freed from salts and chemicals in water and kept in a refrigerator for 24–48 hours. The extract is then filtered through paper, asbestos or a Seitz pad, and, if necessary, neutralized. High-titre lyophilized sera are advised to avoid non-specific reactions. Sera with a titre of 1/4,000 to 1/8,000 were used in the proportion of 0·1 serum to 0·9 extract—these were observed for 30 minutes in tubes 5 mm. in diameter.

These methods were tested on sausages of known composition giving results as expected. This was not the case when 50 samples from the open market were examined but it was likely that the meats used were not those stated by the manufacturers. In one case a reaction suggesting the use of mutton was possibly due to the use of sheep's milk. It is suggested that a wider use of the method and the resulting experience would make of it a practicable measure. *E. Agius*

SANTOPADRE, G. & DELL'OMODARME, G. In merito al problema del controllo igienico dell'industria e del commercio dei molluschi eduli. [**On the Problem of the Hygienic Control of the Edible Shell-Fish Industry**] *Ann. d. San. Pubblica.* Rome. 1958, July–Aug., v. 19, No. 4, 791–9, 1 graph. [24 refs.] English summary.

On the basis of answers to a questionnaire and a study of data from the Italian Central Institute of Statistics, the authors show that there is a clearly greater incidence of enteric diseases and a greater proportion of them attributable to consumption of shellfish in coastal than in inland towns, these latter figures varying from 75% in Leghorn and Savona to 5 and 1% in Vicenza and Verona. Out of 59 laboratories which answered the questionnaire only 15 had been asked to examine shellfish within the few preceding years, and this far from regularly. It appeared that shellfish coming from authorized nurseries were put on the market without any bacteriological controls, the authorities concerned relying solely for their judgment on the situation of the shellfish beds, laboratory control being advised but not prescribed by law. It is believed that the only practicable way of improving an undesirable state of things would be the introduction of compulsory purification of shellfish. *E. Agius*

DÍEZ MARTÍN, C. Estudio de los sistemas de depuración de moluscos. (Ostras, almejas y mejillones). [**A Study of Shell-Fish Purification Methods: Oysters, Clams, and Mussels**] *Rev. Sanidad e Hig. Pública.* Madrid. 1958, Mar.–Apr.–May, v. 32, Nos. 3, 4 & 5. 187–229.

In Spain legislation on shellfish consists of an order of 30 March 1953 regulating shellfish nurseries, and of the order of 10 March 1956 which completes and amplifies it, enforcing registration, grading and surveillance of shellfish beds and of the conditions of marketing.

Brief references are made to the historical aspects of the consumption of molluscs and their use in folk medicine. 100 grammes of oysters, clams and mussels yield 80, 81 and 88 calories, respectively. They are useful sources of amino-acids, mineral salts (including iron and copper), glycogen, iodine, etc. PONGET is quoted as proving that a kilogramme of oysters is equal in value to a litre of milk. They are the richest of all foodstuffs as a source of iodine. Clams and mussels are also very rich in mineral salts, especially in phosphorus and iodine.

Mussels are the molluscs most abundantly cultivated on the beaches of Corunna, both in natural and artificial breeding grounds, oysters and clams being reared almost solely in natural beds. Mussels are in increasing demand, while oysters appear to be declining in popularity. Production from these nurseries varies with size, 25,000 to 30,000 kgm. being an average figure [presumably yearly]. Orders from abroad, especially from France, could not be filled as there were not enough purification centres which could issue the necessary certificate. More such stations would open up new markets.

Pathogenic micro-organisms (salmonellae, shigellae, vibrios, etc.) have often been associated with molluscs. Cases of intoxication have been ascribed to a toxic substance referred to as mytilotoxin, but toxicity has now been found to be due to the presence of dinoflagellates, in many studies carried out in California, Belgium, Canada, etc. These dinoflagellates, owing to ecological disturbances, can become abnormally abundant in the plankton, producing the condition known as red water or red tide, *eaux rouges, purga del mar* or *ardor del mar*, together with an increased luminosity. This condition is lethal for fish, crustaceans and molluscs, but a less marked predominance of dinoflagellates can occur in which only molluscs are affected, becoming toxic for human consumers. Mytilotoxin appears to be more toxic than potassium cyanide, strychnine or curare, strong doses producing immediate paralysis of the respiratory muscles. It is very difficult to remove this danger, the usual methods of purification not being effective. Continual observation of the plankton appears to be the only practicable precaution.

The rest of the article is dedicated to the study of the

relations of molluscs with pathogenic bacteria. Salmonellae have a special power to persist in the bivalves, and show an almost absolute resistance to their destructive forces. An experiment by the author on artificially infected oysters and mussels showed that while 80% still gave evidence of the presence of *Salm. typhi* after 24 hours, almost all were free after 90 hours when lying in water at 15°C., though they were still infected after 28 days at 1°C. Sea water normally frees itself of germs, infection of molluscs being always determined by the proximity of man.

The hygienic control of molluscs basically depends on estimation of faecal pollution through the presence of *Escherichia coli*. The method adopted was culture on lactose broth, with passage on to Levine's eosinmethylene blue agar, further identification being carried out by the usual methods. Streptococci were sought by glucose broth cultivation. The methods in use for estimation of *E. coli* in molluscs are those described by EYRE, by HANSTON, by BIGGER, those laid down by the Middleburg conference and the standard American method. The author prefers Bigger's method, which again consists in inoculating various dilutions in liquid peptone-bile-salt-lactose medium. Possibility of infection is suggested when out of any 10 molluscs at random 7 show the presence of presumptive *E. coli* in tubes seeded with 0·5 ml. of the triturated mollusc, or 3 in the tubes seeded with 0·1 ml. or 1 in tubes seeded with 0·1 ml. or 1 in tubes seeded with 0·02 ml. The Middleburg method introduces the use of a solid medium containing erythrosin and methylene blue. Counts can be made on this medium. The standard American method is carried out on the water contained in the mollusc. Most authorities agree that estimation of streptococci and anaerobes are of little or no practical importance.

Since molluscs free themselves of pathogens in 4 days any method which keeps them in bacteriologically clear water for that time will be satisfactory, and methods depend on ways of purification of the water used. One method simply relies on keeping the molluscs in the open sea in floating cleansing tanks for 3 days. These have to be at least 10 miles away from the coast. This method is used only in Japan.

A method of which the author is very hopeful depends on the use of ultra-violet lamps as sterilizing agents. This method is used at a station at Tarragona. Other methods depending on filtration, X-rays, irradiation by uranium derivatives and supersonic vibrations are not considered practicable as yet.

Among chemical methods, many cannot be used since they affect the taste or vitality of the molluscs or because they are too expensive, and chlorination is the only method in use. Chlorine can be obtained by electrolysis from the sea water or from sodium or calcium hypochlorite. The 2 most interesting methods of chlorination are Dodgson's in which chlorine is used at a concentration of 3 parts per million, and Wells's method based on the fact that when molluscs are treated with an excess of chlorine they close their shells and for a time the chlorine acts solely on the outside, the shells only reopening as the concentration drops, when they are transferred to tanks in which chlorine is at a concentration of 2 parts per million, Wells's method alters the taste of the molluscs and has not been used much.

A detailed description is given of the apparatus and working of the oyster purification plant at Brightlingsea and Conway in Great Britain and of that on the Tagus at Moita in Portugal. They are both very similar, the British plant using calcium hypochlorite while the Portuguese uses sodium hypochlorite and chlorine at a slightly stronger concentration. The author carried out a test using calcium hypochlorite and obtained completely satisfactory results. A small scale trial of quaternary ammonium compounds showed that, while these were effective in sterilization, the vitality of the molluscs and their taste were adversely affected. The process is also rather expensive. Views on the practicability of using ozone are conflicting, but the author thinks that good results could be obtained.

The possibility of using broad spectrum antibiotics was considered and a test was carried out with a mixture of oxytetracycline and aureomycin containing 986 units per mgm. in dilutions which gave a final concentration of 5 and 2·5 parts per million. This showed both concentrations to be effective, not affecting the molluscs' vitality or their taste. Residual quantities of antibiotics were less than 1 unit per ml. Purification by antibiotics would be excellent but the inherent difficulties are really prohibitive.

An estimate of the cost of purification by chlorine at a suggested station works out at 20 centimos [less than one penny] per kgm.

[This article provides a useful survey of many practical aspects of shellfish work.] *E. Agius*

BEARNS, R. E. & GIRARD, K. F. **The Effect of Pasteurization on** *Listeria monocytogenes*. *Canadian J. Microbiol.* Ottawa. 1958, Feb., v. 4, No. 1, 55–61, 2 figs. [16 refs.]

L. monocytogenes is an organism with considerable heat tolerance and it has been suggested that it may possibly be pathogenic to man. In the experiments recorded here it was found that when the organism was added to sterile milk and subjected to holder-type pasteurization for 35 minutes at 61·7°C. there was survival whenever the initial number of bacteria added was 5×10^4 ml. or greater. After 48 hours at room temperature (22°C.) the survivors multiply and viable bacterial counts may reach 10^8 per ml. and this without producing any gross detectable changes in the milk.

This organism has been isolated from raw milk but little is known as to its relative frequency in such milk.

W. G. Savage

FOOD POISONING

PUBLIC HEALTH LAB. SERVICE. **Food Poisoning in England and Wales, 1957. A Report.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, Nov., v. 17, 252–63. [14 refs.]

As usual this report is packed with interesting and valuable information. For 1957 there was a reduction

of 8% on the previous year, the total incidents being 7,071. This reduction was mainly in incidents involving *Salmonella typhimurium*. Salmonella strains were responsible for 4,218 incidents (59%), staphylococci 128 (2%), *Clostridium welchii* 93 (1%), other causes 7, and in 2,625 incidents (37%) the cause was not ascertained.

These incidents were divided into 473 general outbreaks, 501 family outbreaks and 6,097 sporadic cases from about 15,100 cases reported. The fatal cases reported were 36, all but 3 (*Cl. welchii*) being associated with salmonella strains.

2 interesting tables summarize the vehicles responsible. Table 4 deals with vehicles and causal agents in 200 general and family outbreaks for which information is available. For salmonellae the vehicles were fish 2, meat 10, sweetmeats 4, eggs 6 (4 being duck), cheese 1. With staphylococci the striking feature is that of 66 incidents 36 were associated with processed and made-up meat while 16 were due to canned vegetables (all processed peas). The 59 *Cl. welchii* incidents were nearly all (54) associated with processed and made-up meat foods. Only 6 incidents were from eggs and all were due to salmonellae. Table 5 includes the 1957 food poisoning outbreaks (including family outbreaks) associated with processed or made-up meats. 137 outbreaks are included. Of these 40 were associated with reheated meat of various kinds and all but one of those ascertained were due to *Cl. welchii*. In the meat pies group causal agents were *Cl. welchii* 16, salmonellae 1, staphylococci 3, other organisms 1 and not discovered 10. Staphylococci were almost all associated with cold ham or boiled bacon and these organisms were the causal agents for 8 out of 10 of the "brawn, meat in gelatin, meat roll, potted meat" group.

In all 17 of the outbreaks associated with vegetables the vehicle incriminated was canned peas, mostly of one brand and in 6 lb. cans. The *Staphylococcus aureus* isolated were mostly of type 42E. Defective cans and infection through leaks are suggested as the probable methods of infection. It is of interest that since 1949 no outbreaks associated with milk are reported. Data are supplied as to the rise and fall of different types of salmonellae in food poisoning incidents which is linked probably with the use of different types and different sources of foods, foreign imported eggs being a definitely ascertained factor.

Analysis of the processed or reheated meat dishes incriminated in salmonella outbreaks over the past few years shows that nearly two-thirds have been pork pies, brawn, sausages and cold pork. Reference is made to a number of investigations showing the high percentage of pigs which may be infected with salmonellae in slaughterhouse premises. This links up with the presence of salmonellae in animal feeding stuffs and fertilizers. Together they offer a valuable line of control over the problem of the distribution of these organisms.

[For the 1956 Report, see this *Bulletin*, 1958, v. 33, 499.] *W. G. Savage*

SKULBERG, A. **A Case of Fish-Borne Type B Botulism.** *Nordisk Hyg. Tidskr.* 1958, v. 39, Nos. 9/10, 133–6. [17 refs.]

A single case was diagnosed clinically mainly on the result of ophthalmological examination. This was confirmed by the isolation of *Clostridium botulinum* type B and by confirmation of toxin in the serum. The vehicle was "rakefisk", a Scandinavian dish, prepared by placing fresh trout in layers with salt and sometimes a small amount of sugar in a tub and with pressure on top of the fish. The tub is stored in a cool place and the fish is served uncooked. When eaten the food had an unpleasant smell and only a small portion was eaten. The clinical symptoms are not described and apparently the patient recovered. Points of interest are that this case and 5 of the 7 cases of botulism (due to meat) previously reported in Norway and bacteriologically investigated were due to *Cl. botulinum* B; no E group, which nearly always has fish for its vehicle, was found. Although the food was putrescent when eaten no other clostridia were isolated. The toxic content of the patient's blood was low and the toxin tested on mice was of comparatively low toxicity. This is the first fish-borne outbreak of botulism reported in Norway. *W. G. Savage*

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

GINTSCHEFF, P. Z. Neue Differentialnährböden für die laufenden Untersuchungen. [**New Media for the Differentiation of Bacteria in Routine Examination**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 124–8.

3 media are described—a solid medium for differentiation of pathogenic and other bacteria in the plating of stools, a basic fluid medium for determining fermentation of sugars, etc., and a medium containing urea and saccharose for immediate differentiation of *Corynebacterium diphtheria, C. xerosis* and pseudodiphtheria bacilli.

The formulae for these media are given: the chief point is the use of a mixture of "Wasserblau" and phenol red which provides a particularly sharp indicator —bright brown at *p*H 7·2, green in acid and red in alkaline solutions. *J. W. McLeod*

ANNEAR, D. I. **Observations on drying Bacteria from the Frozen and from the Liquid State.** *Australian J. Exper. Biol. & Med. Sci.* 1958, June, v. 36, Pt. 3, 211–21, 3 figs.

A new method of drying suspensions of bacteria kept in the liquid state is described and the results compared with more conventional methods of drying from the frozen state. To prevent the material freezing ampoules were placed in a water-bath (generally at room temperature) which allowed rapid transfer of heat from the water outside to that in the ampoules. Under vacuum evaporation was rapid, *e.g.* at 20°C. the material appeared to be dry within 2 minutes, and at 30°C. within 1 minute. The suspending fluids used were various combinations of peptone and glucose.

All methods examined were successful in drying a salmonella serotype and *Vibrio cholerae*, but after 6 months' storage the viable count of the vibrio was only about half that found immediately after drying. Annear believes that enough evidence has been presented to show that peptone can be used in place of serum in the routine drying of stock cultures by the centrifugal freeze-drying method.

[See also this *Bulletin*, 1958, v. 33, 972.]

S. T. Cowan

HOLDEN, H. F. **Apparatus for Vacuum Distillation and for "Freeze-Drying".** *Australian J. Exper. Biol. & Med. Sci.* 1958, June, v. 36, Pt. 3, 285–8, 2 figs.

This short paper is a brief description of 3 pieces of apparatus for biochemists who want to remove water from dialysates and chromatographic eluates, and for bacteriologists who freeze-dry cultures using calcium carbide as the desiccant. The original should be read by those interested. *S. T. Cowan*

SCHMIDT, B., FELDMANN, S. & DOBBERSTEIN, H. Untersuchungen zur Frage der Änderung der biologischen Eigenschaften von Bakterien nach Trocknung und Gefriertrocknung. [**On the Stability of Biological Characters of Bacteria after drying and freeze-drying**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 7/8, 573–80, 2 figs. [21 refs.]

In view of the conflicting claims for simple vacuum drying and freeze-drying as methods of preserving bacteria alive over long periods and the particular difficulties reported in preserving such delicate forms as the gonococcus and the pneumococcus, the authors made a careful parallel investigation of the two methods.

100 strains were used drawn from the genera *Escherichia, Salmonella, Streptococcus pneumoniae, Neisseria, Haemophilus* and some pigment forming strains.

The suspending medium chosen was skim milk and the survival rates in fluid suspensions dried without freezing and of material frozen at various speeds and at different temperature levels were compared.

The general result obtained was that simple drying was at least as good as any of the methods of freeze-drying and considerably better than those involving the lowest temperatures and quickest freezing.

A comprehensive investigation of the biochemical activities and biological chemistry of the strains did not show these to be impaired in any way.

These results cover observations made immediately after the drying process as well as after 6 months at room temperature.

Only one strain was lost, a *Corynebacterium xerosis*: this was attributed to inadequate growth of the culture used at the outset.

The only heavy falls in the number of persisting living forms were with the following:—3 of 6 strains of *Str. pneumoniae*, the gonococcal, the meningococcal and the *H. influenzae* strains. These losses were all with the freeze-dried material except in the case of *Haemophilus* which decreased markedly in both preparations. *J. W. McLeod*

TOMCSIK, J. Feinstruktur der Bakteriengrenzflächen. [**The Ultrastructure of the Marginal Surface of Bacteria**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 5/6, 361–8. [83 refs.]

WINKLER, A. Feinstruktur des Bakterienzellinhaltes. [**The Ultrastructure of Bacterial Cell Contents**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 5/6, 369–75, 3 figs. [23 refs.]

BABUDIERI, B. Die Feinstruktur der Leptospiren und anderer Spirochäten. [**The Ultrastructure of *Leptospira* and other Spirochaetes**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 5/6, 386–406, 22 figs. [53 refs.]

KALINA, G. P. **Bacterial Protoplasts (Review).** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 1/2, 143–57. [Numerous refs.] [Translated from Russian.]

KLIENEBERGER-NOBEL, Emmy. Die L-Form der Bakterien. [**The L Forms of Bacteria**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 5/6, 376–85. [42 refs.]

CÉSAIRE, O. G., NEUZIL, E. & BOIRON, H. Recherches sur le métabolisme azoté microbien. I.—Métabolisme des aminoacides par *Pseudomonas aeruginosa*. [**Studies on the Nitrogen Metabolism of Bacteria. I. Metabolism of Amino Acids by** *Pseudomonas pyocyanea*] *Bull. Soc. Chimie Biol.* 1958, v. 40, No. 11, 1435–46. [30 refs.] II.—Métabolisme des aminoacides par *Salmonella paratyphi B*. [**II. Metabolism of Amino Acids by *Salmonella paratyphi B***] *Ibid.*, 1447–52.

HOROWITZ, J., LOMBARD, Anna & CHARGAFF, E. **Aspects of the Stability of a Bacterial Ribonucleic Acid.** *J. Biol. Chem.* 1958, Dec., v. 233, No. 6, 1517–22, 3 figs. [19 refs.]

HUANG, H. T. & DAVISSON, J. W. **Distribution of Lysine Racemase in Bacteria.** *J. Bacteriology.* 1958, Nov., v. 76, No. 5, 495–8.

NORTH, E. A. & DOERY, Hazel M. **Protective Action of Venoms containing Phosphatidase-A against certain Bacterial Exotoxins.** [Correspondence.] *Nature.* 1958, Nov. 15, v. 182, 1374–5.

The crude venom of Australian black snake (*Pseudechis porphyriacus*), king brown snake (*Pseudechis australis*), and the honey bee (*Apis mellifera*) like the haemolysin-rich fraction of the Australian tiger snake venom (*Notechis scutatus scutatus*) [this *Bulletin*, 1958, v. 33, 884] protected mice against the lethal action of staphylococcal toxin. These 3 venoms are also strongly haemolytic and contain the enzyme phosphatidase-A.

Toxoided haemolysin-rich fraction of tiger snake venom was less toxic than untoxoided material but still protective when given up to 30 minutes after staphylococcal toxin; this material and crude bee venom also protected mice against intraperitoneal challenge with living staphylococci.

Phosphatidase-A splits lecithin to fatty acid and lysolecithin. The authors report the neutralization of staphylococcal alpha toxin, tetanus toxin and diphtheria toxin by sodium oleate or sodium linoleate and the protection against the lethal action of staphylococcal toxin in mice by sodium oleate; the haemolysin-rich fraction of tiger snake venom is antagonistic to the action of tetanus toxin in mice. *M. Patricia Jevons*

DOLD, H., REIMOLD, G. & DAMMINGER, R. Die Entwicklung der Keimflora in der Mundhöhle der Neugeborenen. [**The Development of the Oral Bacterial Flora in the Newborn Infant**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 69–76. [12 refs.]

Frequent examinations were made to determine the bacterial flora of the mouth of infants in the first few hours after birth. Infants born naturally commonly harboured in their mouths, immediately after birth, organisms similar to those in their mothers' vaginas. Infants born by caesarean section commonly had sterile mouths at birth. Infants whose mouths were sterile at birth were usually colonized by the time they were 10–15 hours old, most often with α-haemolytic streptococci. *R. E. O. Williams*

TORLONI, M. & BORZANI, W. **A Filtration Method for the Determination of Concentration of Micro-organisms in Air.** *Applied Microbiol.* Baltimore. 1958, July, v. 6, No. 4, 252–4, 8 figs.

The air sampling method described employs filter paper as the collection medium; after exposure fluid culture medium is added to the filter paper which is incubated *in situ* and the developing colonies are counted. [The tests of the apparatus that are reported are quite inadequate and, in particular, do nothing to substantiate the authors' claim that it can be used for long period sampling.] *R. E. O. Williams*

DECKER, H. M., KUEHNE, R. W., BUCHANAN, L. M. & PORTER, R. **Design and Evaluation of a Slit-Incubator Sampler.** *Applied Microbiol.* Baltimore. 1958, Nov., v. 6, No. 6, 398–400, 3 figs.

"A sampler has been designed which permits continuous sampling of vegetative organisms with a high degree of efficiency. The organisms in the air are collected on a selective agar in a stainless steel tray which passes under a slit opening located in the top of the sampler. A unique feature is the incorporation of an incubator chamber which is automatically turned on at the completion of sampling, requiring attendance of the sampler only once in a 24-hr period. Civilian defense agencies, hospitals, and research laboratories can utilize this sampler for time-concentration detection of microorganisms in the atmosphere. Air-borne transmission of disease over long time periods should be traced more readily by the use of this sampler."

HAMMOND, E. C. **Ammonium Alginate Wool as a Filter for collecting Micro-Organisms from Large Volumes of Air.** *J. General Microbiol.* 1958, Oct., v. 19, No. 2, 267–70, 2 figs.

Aluminium alginate wool [this *Bulletin*, 1956, v. 31, 65] (50 denier/12 filament) was found to act as an efficient filter for bacterial sampling when tested against a sprayed suspension or a dust of *Bacillus subtilis* spores in comparison with a membrane filter in tandem. For cultivation the wool was dissolved in 0·5% dipotassium hydrogen phosphate solution. [Neither the volume of air sampled, nor the duration of sampling is given explicitly, nor is the arrangement of the 2 samplers described with sufficient detail to enable an assessment of the figures. In the reviewer's experience some samples of alginate wool, when dissolved in buffer, prove inhibitory to some bacteria.] *R. E. O. Williams*

HARPER, G. J., HOOD, A. M. & MORTON, J. D. **Air-borne Micro-Organisms: a Technique for Studying their Survival.** *J. Hygiene.* 1958, Sept., v. 56, No. 3, 364–70.

For any study of the survival of bacterial cells suspended in air it is necessary to distinguish between loss from settling and other physical causes, and death. One method that has been used for this purpose is to mix a suspension of spores with the test organism under study, the spores being regarded as a stable tracer, subject only to the physical effects. Some experiments showed, however, that dispersal of a spore suspension as an aerosol could result in conversion of a large proportion to a heat-sensitive form. It was found better, therefore, to use killed radio-active cells as the tracer, and for preference cells of the particular species under study. *R. E. O. Williams*

FERRY, R. M., BROWN, W. F. & DAMON, E. B. **Studies of the Loss of Viability of Bacterial Aerosols. III. Factors affecting Death Rates of Certain Non-Pathogens.** *J. Hygiene.* 1958, Sept., v. 56, No. 3, 389–403, 6 figs.

Ferry and his colleagues have already reported some of their studies on the decay rate of bacterial aerosols held in a balloon for varying periods [this *Bulletin*, 1958, v. 33, 683].

They have now found that storage of the aerosol in nitrogen instead of air leads to slowing of the secondary decay stage with *Micrococcus* [*Staphylococcus*] *candidus*, *Escherichia coli* and *Serratia marcescens* [*Chromobacterium prodigiosum*]; this supports the idea that the secondary stage is due to oxidative processes. The immediate decay rate of *E. coli* was not affected by storage in nitrogen. The secondary decay of *M. candidus* was increased by a rise in temperature. Attempts were made to cover the surface of the bacteria with polyatomic alcohols; this did not decrease the primary decay rate and may have increased it.

R. E. O. Williams

LOWBURY, E. J. L. & LILLY, H. A. **Contamination of Operating-Theatre Air with** *Cl. tetani*. *Brit. Med. J.* 1958, Nov. 29, 1334–6, 1 fig. [10 refs.]

Clostridium tetani was isolated from air samples with the use of a large slit sampler collecting on to gelatin plates, which were subsequently melted and added to cooked meat broth. After 4 and 12 days' incubation smears were examined for characteristic bacilli and, if these were present, the broth was subcultured to a Fildes agar slope. Toxigenicity was tested either by injection of mice, or inoculation of a blood agar plate, half of which had been spread with antitoxin; haemolysis by *Cl. tetani* was neutralized by the antitoxin.

Cl. tetani was isolated from 24 of 27 air samples taken in the road and 33 of 50 taken in an exhaust-ventilated operating theatre; it was not isolated from any of 23 samples taken in a burns dressing station ventilated under positive pressure with filtered air. The organism was also isolated from garden soil, ward floor and street dust, trouser turn-ups and human faeces.

R. E. O. Williams

KINMONTH, J. B., HARE, R., TRACY, G. D., THOMAS, C. G. A., MARSH, J. D. & JANTET, G. H. **Studies of Theatre Ventilation and Surgical Wound Infection.** *Brit. Med. J.* 1958, Aug. 16, 407–11, 7 figs. [11 refs.]

The authors investigated a pair of twin operating theatres at St. Thomas's Hospital, London. Both were ventilated under positive pressure by a plenum system providing filtered air. During the investigation 1 had the air inlets altered so as to give a cross-draught of approximately 150 feet per minute at the operating table, while the other remained with general turbulent mixing but no detectable draught at the table.

The change of air direction reduced the average bacterial count of air sampled near the wound during operation from 21·7 to 9·9 colonies per cu. ft. Further very slight reductions in the count were achieved by having all members of the surgical team change all their clothes for operating, and by the installation of a new door to improve the positive-pressure effect.

The incidence of sepsis in all patients having clean operations in the 2 theatres was observed during the 3 years 1955–7. The incidence of minor sepsis was 6·3%, 5·7% and 7·4% and of severe sepsis 2·9%, 4% and 3·4%, in the 3 years respectively. The changes in air supply, etc., which reduced the bacterial count in the air, had no detectable effect on the incidence of sepsis. Nor could any relation be found between sepsis and the presence of *Staphylococcus aureus* in the theatre air.

Many of the cases of severe sepsis were, nevertheless, probably due to infection introduced at the time of operation. Sources of infection other than the air, especially the patient himself, are discussed.

R. E. O. Williams

SOMPOLINSKY, D. **On the Influence of Antibiotics on Air Bacteria in an Operating Theatre.** *Acta Med. Orientalia.* 1957, Sept.–Oct., v. 16, Nos. 9/10, 222–7, 1 fig.

Culture plates were exposed to collect bacteria settling from the air in an operating theatre in a hospital in Israel. The mean count, per sq. metre, during operations was 53,000. This is higher than reported by several other authors. Rules were therefore introduced forbidding anyone to enter the operating theatre building without donning cloth overshoes. The average settle-plate count thereafter was 15,181 colonies per square metre. Culture media containing penicillin or streptomycin or both were also exposed. The counts on these plates were much lower than those on nutrient agar plates, but the proportion of pathogenic bacteria was higher.

R. E. O. Williams

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order: General; Antibiotics; Other Therapeutic Substances; Disinfection.

WATERWORTH, Pamela M. **Spurious Growth Inhibition by Antibiotic Discs having a Lactose Base.** *J. Med. Lab. Technol.* 1958, Oct., v. 15, No. 4, 245–8, 1 pl.

In a primary culture to which an Evans Sentest disk (tablet) containing penicillin had been applied, growth of *Pseudomonas pyocyanea* was inhibited in a wide zone surrounding the disk, but the growth of *Staphylococcus pyogenes* accompanying it was unaffected. The same result was obtained with a "control" disk containing no antibiotic. The base of these disks is lactose, and it therefore appeared that the fermentation of lactose by staphylococci produces a substance inhibiting the growth of *Ps. pyocyanea*. *Streptococcus faecalis* was found to be even more active in producing it, and other Gram-negative bacilli including some but not all species of *Salmonella* tested, and some species of

Proteus and *Klebsiella* were inhibited by it. The inhibitory substance, which was also formed from glucose and other sugars, could not be certainly identified: of 6 acids and 8 other possible products of fermentation only propionate inhibited *Ps. pyocyanea* in a much lower concentration than that inhibiting *Str. faecalis*.

It is pointed out that on a medium containing lactose the growth of one of two organisms in material such as urine may be suppressed, and secondly that lactose is an unsatisfactory base for antibiotic disks: an inert substitute should be found for it. *L. P. Garrod*

Mohberg, Joyce & Johnson, M. J. **Comparative Study of the binding of Synnematin and Penicillin by Bacterial Cells.** *J. Bacteriology.* 1958, Oct., v. 76, No. 4, 385–92, 4 figs. [14 refs.]

These authors prepared penicillin and synnematin containing ^{35}S, exposed suspensions of *Staphylococcus aureus* to solutions of these antibiotics, and determined the degree of radio-activity of washed cells which had been so treated. The amount of either antibiotic bound was independent of concentration above a certain level, and the amounts were almost the same, $7{\cdot}8 \times 10^{-3}$ and $8{\cdot}0 \times 10^{-3}$ μmoles of synnematin and penicillin respectively per gm. of cells. The degree of radio-activity was little affected by subsequent suspension either in buffer solution or in non-radioactive antibiotic solution, whether the same or the other antibiotic [in column 2 of Table 2 the "incubating solutions" are incorrectly, according to the text, stated to have been radioactive]: these results suggest that the two antibiotics are bound at the same site. There was a great difference in the rate of binding, that of penicillin being 28·5 to 69 times more rapid, a fact which may perhaps be connected with its greater antibacterial activity.

L. P. Garrod

Lightbown, J. W., Mussett, M. V. & Suilitzeanu, D. **A Method for the Blood-Serum Assay of the Blood-Level Duration Test for Oily Injection of Procaine Penicillin.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 6, 1085–91.

Jay, J. M., Weiser, H. H. & Deatherage, F. E. **The Inhibition in Beef of Chlortetracycline-Resistant Bacteria by Sub-Bacteriostatic Concentrations of the Antibiotic.** *Applied Microbiol.* Baltimore. 1958, Sept., v. 6, No. 5, 343–6.

Jay and his colleagues have previously shown that all 3 tetracyclines inhibit the growth of *Proteus vulgaris* and *Pseudomonas pyocyanea* in beef in a concentration of 5 p.p.m., whereas that necessary to do so in broth is 50 p.p.m. (*i.e.*, 50 μgm./ml.). There is no such difference in the action of penicillin, streptomycin or chloramphenicol. In this paper these observations are extended. The tests were made with suspensions of fresh beef in water prepared in a Waring blender, with or without the addition of 5 and 10 p.p.m. of chlortetracycline and inoculated with small numbers of 1 of these species of organism: viable counts were made after 1, 2 and 3 days (the temperature at which the suspensions were kept is not stated). In the presence of the antibiotic the organisms multiplied very little or diminished in numbers: in its absence they multiplied, but to a variable but usually moderate extent. On the other hand, if the meat had been roasted before the suspension was made, or if the suspension itself was heated to 100°C. for 30 minutes, growth was profuse whether the antibiotic was added or not. Heating to 90°C. did not have this effect: hence the change caused by cooking cannot be due to the destruction of complement or properdin. When the meat suspension was prepared in normal saline instead of water the inhibiting effect of chlortetracycline was abolished. The authors explain the effect as due to the release by cooking of nutrients which are unavailable in raw meat. [Although this could perhaps not wholly explain the effect, it is surprising that nothing is said about the *p*H of the meat suspensions. Chlortetracycline is much more active, because more stable, in an acid than an alkaline medium.] *L. P. Garrod*

Kunin, C. M. & Finland, M. **Demethylchlortetracycline. A New Tetracycline Antibiotic that Yields Greater and More Sustained Antibacterial Activity.** *New England J. of Med.* 1958, Nov. 20, v. 259, No. 21, 999–1005, 2 figs.

A mutant of *Streptomyces aureofaciens* has been found to produce some new forms of tetracycline "highly resistant to degradation by acid and alkali", and including 7 - chloro - 6 - demethylchlortetracycline (DMCT), which is the subject of this paper. 2 capsules each containing 250 mgm. of the hydrochloride of this substance and of tetracycline, the latter also containing citric acid to promote absorption, were given to normal subjects, and the antibiotics were assayed in the blood at intervals. Of the organisms used in assays *Bacillus cereus* was 4, a streptococcus 2 and a staphylococcus 1·5 times more sensitive to DMCT than to tetracycline. The results both of these and of experiments in which the initial 500 mgm. dose was followed by further 250 mgm. doses at 12-hour intervals are given very fully in both tables and graphs. The blood level attained by DMCT diverges from that of tetracycline at about the third hour and remains at a considerably higher level (×2 or more) up to the 24th hour: in each of 8 subjects DMCT was still detectable after 72 hours (0·1–0·7, average 0·3, μgm./ml.). During repeated administration, the concentrations attained in the blood by DMCT were sustained at a considerably higher level than those of tetracycline, with some evidence of cumulative effect. The renal clearance of DMCT was shown to be more than twice as slow as that of tetracycline. [It is not clear whether this fact, or better absorption, possibly due to greater stability, is believed to account for longer persistence of DMCT in the blood. The findings are complicated by the use of 3 different organisms for assays, and by statement with and without correction for the differing sensitivity of each organism to the 2 drugs. It is nevertheless clear that the degree of antibacterial activity produced in the blood by DMCT is considerably greater than that produced by tetracycline.]

L. P. Garrod

VOGEL, R. A. & CRUTCHER, J. C. **Studies on the Bioassay and Excretion of Amphotericin B in Patients with Systemic Mycoses.** *Antibiotic. Med.* New York. 1958, Aug., v. 5, No. 8, 501–6, 2 figs.

2 patients, one with histoplasmosis and one with cryptococcosis, each involving the meninges, were treated with amphotericin B administered intravenously for several months. 2 assay methods were used for determining the concentration of the drug in the blood and urine: that employing *Candida albicans* was more rapid, and that employing *Histoplasma capsulatum* slower but more sensitive. The course of treatment was complicated by alterations in dose and frequency of administration and by changing from an "insoluble" to a "water soluble" form of the drug [according to a note on a reprint kindly supplied by the authors, details about this treatment in the legend of Fig. 2 should have been printed under Fig. 1]. Fluctuations in blood levels in both patients are presented in a composite graph: chronological data on the abscissa are entirely illegible in places, but it is evident that at about the time when treatment was changed to the soluble form of the drug, much higher levels were attained. Excretion of diminishing amounts in the urine continued in 1 patient for 2 months after treatment was stopped. The blood urea rose in both patients during treatment, but fell to normal later. Both patients improved during treatment, but "are still under critical observation". *L. P. Garrod*

CHICK, E. W., EVANS, J. & BAKER, R. D. **The Inhibitory Effect of Amphotericin B on Localized *Rhizopus oryzae* Infection (Mucormycosis) utilizing the Pneumoderma Pouch of the Rat.** *Antibiotics & Chemotherapy.* New York. 1958, Oct., v. 8, No. 10, 506–10, 5 figs.

A "pneumoderma pouch" is produced by injecting 25 ml. of air subcutaneously in the mid-scapular region of a rat. This air-containing cavity was inoculated with 1 ml. of a spore suspension of a strain of *Rhizopus oryzae* isolated from a fatal case of mucormycosis. Half the rats so inoculated also received an injection into the cavity of 15 mgm. of amphotericin B in 1 ml. of water. They were killed after 5, 9 and 18 days and the borders of the cavity examined histologically. The cellular reaction was similar in control and treated groups, except that leucocytic infiltration was more marked at an early stage in the latter. In the control group the fungus proliferated and formed hyphae, but in the treated, with a single minor exception, no fungus was seen except the spores originally introduced.
L. P. Garrod

GRIFFITH, R. S., STEPHENS, V. C., WOLFE, R. N., BONIECE, W. S. & LEE, C. C. **Preliminary Studies on Propionyl Erythromycin.** *Antibiotic Med.* New York, 1958, Oct., v. 5, No. 10, 609–13, 2 figs. [15 refs.]

These workers from the Research Laboratories of ELI LILLY and Co. here report that a study of esters of erythromycin has been made, in which it was found that the propionyl ester produces higher degrees of antibacterial activity in the blood than the base or any other ester examined. This observation is verified here by graphs of mean blood levels in large numbers of subjects ½, 1, 2, 4, 6 and 8 hours after a single 250 mgm. dose of the new ester and of erythromycin base in tablet or capsule form: the ester is absorbed more rapidly, attains a higher peak level and remains at a higher level after 8 hours. Studies in rats showed that very little propionyl erythromycin is excreted in the bile (concentration attained averaged 57 μgm./ml. compared with 992 μgm./ml. for erythromycin base); this may explain the higher levels attained in the blood. When the propionyl ester is given, 80% of the antibiotic excreted in the urine is in this form: hence it apparently acts unchanged in the body. Brief tabulated particulars are given of 19 patients treated with 250 mgm. propionyl erythromycin every 6 hours for various infections with excellent results. Twice this dose was given for as long as 1 month without ill effects.
L. P. Garrod

BRADLEY, S. G. **Interactions between Phosphate and Nystatin in *Candida stellatoidea*.** *Proc. Soc. Exper. Biol. & Med.* 1958, Aug.–Sept., v. 98, No. 4, 786–9.

Candida stellatoidea was trained to increased resistance to nystatin and to sodium arsenate. As judged by rate of fermentation of glucose in the Warburg apparatus, and by capacity for growth on media containing nystatin or arsenate, there was crossed resistance between these 2 substances. The inhibitory effect of both on glucose fermentation was reduced by adding phosphate buffer. These findings suggest the possibility that the action of nystatin is on oxidative phosphorylation. *L. P. Garrod*

BUNN, P. A. & BALTCH, Aldona, with the technical assistance of Olga Krajnyak. **Clinical Experiences with Kanamycin.** *New England J. of Med.* 1958, Oct. 2, v. 259, No. 14, 659–62.

These authors, from Syracuse, N.Y., gave kanamycin in 0·5 gm. intramuscular doses 3 or 4 times a day to 25 patients, brief particulars of whose illnesses are tabulated. 15 had staphylococcal infections, 6 with positive blood cultures: the diagnosis was primary pneumonia in 4, acute endocarditis in 1, acute pericarditis in 1, osteomyelitis in 2 and abscesses in various situations in the remainder. The other 10 patients had Gram-negative bacillary infections (*Escherichia coli, Proteus* or *Pseudomonas pyocyanea*) causing urinary tract infections in 6, urinary tract infections with pneumonitis in 2, pneumonitis in 1 and abscess in 1: 3 of these patients had positive blood cultures. The longest period of treatment was 21 days, the usual 7–9 days. 2 patients in the second group and 1 in the first died, causes other than the infection contributing: about half the total responded rapidly to treatment and the remainder less convincingly. There is no mention of any toxic effects. The authors are gratified with the results. They warn users that treatment should be based on *in vitro* sensitivity tests [but do not mention having done any themselves]. *L. P. Garrod*

WEBER, R. W. **Staphylococcic Endocarditis treated with Ristocetin.** *J. Amer. Med. Ass.* 1958, Nov. 8, v. 168, No. 10, 1346–51, 4 figs.

This paper describes 2 cases of staphylococcal septicaemia, believed to be complicated by endocarditis, and successfully treated with ristocetin. In a woman aged 32 the apparent origin of the infection was septic abortion: the staphylococcus recovered in each of 8 (!) blood cultures made within 12 hours of admission, was resistant to penicillin and to novobiocin and sensitive to erythromycin and ristocetin. She was treated for 2 days with novobiocin and for about 15 with erythromycin without adequate effect: ristocetin was then given in addition to erythromycin and recovery followed. [Endocarditis was thought to involve the tricuspid valve, but the evidence of it seems uncertain.] The history of the second case, which starts with 2 gynaecological operations, is confused: the first mention of a demonstrable septic focus is the development of abscesses in both antecubital fossae. The organism eventually cultivated from the blood was resistant to penicillin and sensitive to novobiocin, erythromycin and ristocetin. The patient was treated successively with penicillin, novobiocin and erythromycin and ristocetin together, and although her temperature did not reach normal for some weeks, she recovered. The evidences of an endocarditis were a rheumatic history, petechiae and an aortic murmur.

It is noteworthy that in each patient erythromycin continued to be given during and after ristocetin administration. 0·5 gm. ristocetin was given intravenously at 6-hour intervals for most of each course: the total amounts given were 44 and 42 gm. There was considerable difficulty with thrombophlebitis, and both patients developed a severe neutropenia (complete blood counts were done daily with a few omissions and the results are the basis of admirably detailed charts): the polynuclear count rose again when ristocetin administration was stopped. *L. P. Garrod*

VERWEY, W. F., WEST, Margaret K. & MILLER, A. Kathrine. **Laboratory Studies of Streptogramin.** *Antibiotics & Chemotherpy.* New York. 1958, Oct., v. 8, No. 10, 500–505.

This paper is from the Merck Institute for Therapeutic Research. It states the minimum inhibitory concentrations of streptogramin for various bacteria, including multiple strains of staphylococci and several species of streptococci, which, with *Corynebacterium diphtheriae*, are the most susceptible organisms. Therapeutic studies in mice were confirmatory, and showed that the route of administration greatly affected the dose required for protection: this was smallest by the intraperitoneal route, and largest (×93 for streptococcal and ×2,000 for staphylococcal infection) by the intramuscular, showing that the antibiotic is not well absorbed from muscle: values for oral and intravenous routes were intermediate. Some tests of toxicity were also done and are related to the therapeutic findings. Therapeutic tests by local application to wounds infected with staphylococci on rabbits' ears gave highly satisfactory results. Very little of the antibiotic could be detected in the plasma or urine of animals given it by intraperitoneal or intravenous injection. Similarities are pointed out between streptogramin and staphylomycin. *L. P. Garrod*

WALLACH, D. P. & WAGNER, J. G., with the technical assistance of N. J. CRITTENDEN & W. C. BELL. **Studies on the Biological Disposition of Streptovaricin (Dalacin), a New Antibiotic.** *J. Pharmacol. & Exper. Therap.* 1958, Sept., v. 124, No. 1, 16–24, 2 figs.

This paper from the Research Laboratories of the UPJOHN Company describes an elaborate pharmacological study of streptovaricin, a recently discovered antibiotic active *in vitro* and *in vivo* against *Mycobacterium tuberculosis* [this *Bulletin*, 1957, v. 32, 802]. Among its physical properties briefly described is instability in alkaline media: almost all activity is lost in 3 days even at *p*H 7·8. The experiments were made with dogs, and the method for assaying the antibiotic in blood involved extraction of serum with chloroform in the cold and evaporation to dryness. Streptovaricin is absorbed from the alimentary tract: experiments in which it was introduced into tied segments showed good absorption from the small intestine, less from the large and almost none from the stomach. In further experiments it was injected intravenously: serial assays in the blood showed a rapid fall in concentration. This was almost equally rapid in nephrectomized dogs, and assays of urine and bile in other animals proved that only a small proportion of a dose is excreted by these routes. It was also assayed in various organs and no evidence was obtained of concentration or storage in them. It therefore appears that streptovaricin is rapidly destroyed in the body. Satisfactory levels persist in the blood and tissues much longer after oral than intravenous administration, evidently because absorption is gradual. *L. P. Garrod*

SCHUBERT, J. H. & CORNELL, R. G., with the technical assistance of Pamela PELTIER. **Determination of Diphtheria and Tetanus Antitoxin by the Hemagglutination Test in Comparison with Tests** *in vivo*. *J. Lab. & Clin. Med.* 1958, Nov., v. 52, No. 5, 737–43.

The antitoxin content of samples of serum was determined by the agglutination of sheep erythrocytes coated with toxoid after tanning. The concentrated toxoids of the Lederle Laboratories were used.

The sensitivity of the reaction was determined with standard antitoxin of the U.S. National Institutes of Health and found to be 0·0012 unit/ml. for diphtheria and 0·001 unit/ml. for tetanus antitoxins. In the case of the diphtheria antitoxin the results were compared with Schick levels and with intradermal titrations on the skin of the rabbit by the established technique of the Massachusetts State Department of Public Health. The tetanus results were compared with titrations in the mouse.

The general result of these titrations was to show a considerable correspondence with greater sensitivity of the rabbit skin test in the case of diphtheria and the mouse test in the case of tetanus for low concentrations

of antitoxin, and higher sensitivity of the agglutination test where concentrations of antitoxin were considerable, in both conditions. The tests corresponded most nearly where concentrations of antitoxin lay in the range 0·03 to 0·1 in the case of titrations of diphtheria antitoxin.

J. W. McLeod

STUART, L. S., ORTENZIO, L. F. & FRIEDL, J. L. **Variations in Phenol Coefficient Testing.** *Soap.* New York. 1958, Oct., v. 34, No. 10, 79–85, 107–9.

These authors from the Plant Pest Control Division, United States Department of Agriculture, report a study of variability in the results of determining phenol coefficients by the AOAC method (Association of Official Agricultural Chemists). 2 technicians performed the test 25 times on 3 germicides, one being a quaternary ammonium compound and the others phenolic. Variations did not exceed ±6%, and it is accordingly suggested that such products should be labelled as having an activity 12% less than that determined in a series of satisfactory tests. A method of interpreting tests giving "wild plus" and "skip" readings is also proposed. *L. P. Garrod*

WRIGHT, Eleanore S. & SHTERNOV, V. A. **Disinfectant Testing. An Adaptation of the Phenol Coefficient Test Method to** *Mycobacterium tuberculosis*. *Soap.* New York. 1958, Sept., v. 34, No. 9, 95–9, 147. [11 refs.]

Mycobacterium tuberculosis, strain H37Rv, was cultivated as a pellicle on a modified Proskauer and Beck medium with added ox serum: the pellicle was broken up by shaking with glass beads and the culture passed through a 200-mesh stainless steel filter. It was then diluted to a standard opacity and 0·5 ml. was added to 5 ml. disinfectant dilutions at 20°C.: after 10 minutes a 4 mm. loopful was transferred to a tube of the same medium, or medium containing 10% instead of 1% serum. A series of phenol tubes was included in each test, and showed a minimum bactericidal concentration of 1 in 60. Results are given for 8 other phenolic disinfectants, 2 of which were ineffective, ethanol, formaldehyde, an iodophor, a pine oil disinfectant and benzalkonium chloride: the 2 latter were also ineffective. Some detailed results are given showing numerous "wild" tubes. Guineapig inoculation was used as an alternative to culture in a further limited series of experiments. [The authors do not say how coarse were the clumps left after their attempt at homogenization, but presumably variations in the size and the distribution of these account for erratic results. Would not a medium giving dispersed growth be preferable?]

L. P. Garrod

DARMADY, E. M., HUGHES, K. E. A. & JONES, J. D. **Thermal Death-Time of Spores in Dry Heat in relation to Sterilisation of Instruments and Syringes.** *Lancet.* 1958, Oct. 11, 766–9, 3 figs. [10 refs.]

In these experiments tubes containing dried spores were inserted in holes in a block of aluminium insulated except on its lower surface, which was applied to a thermostatically controlled hot plate. Temperature was found to vary very little, and the time taken for a tube to reach the temperature for which the plate was set was 9 minutes: this was therefore deducted from the total time to give the time required for sterilization at that temperature. A sample of dried soil was sterilized at 160, 170, 180 and 190°C. in 90, 70, 15 and 4 minutes respectively: at 150° it was not sterilized in 3 hours. Spores of *Cl. tetani* (2 strains) required 30, 12, 5 and 1 minutes respectively at 150, 160, 170 and 180°C. Spores of *Bacillus stearothermophilus* were killed at 150° in 8 minutes. Tests were also done with Browne's tubes (type iii), said to change colour after 1 hour at 160°C.: this claim was confirmed, and the time required for the change at higher temperatures was correspondingly shorter. It is suggested that rules for dry heat sterilization should be based on findings with *Cl. tetani*, the most heat-resistant pathogen, and that a safety margin should be provided by using a temperature 10° higher than that shown here to be required for a given time of exposure. The recommended holding times are 45, 18, 7½ and 1½ minutes at 160, 170, 180 and 190°C. These findings are compared with those of earlier workers and found to tally reasonably well when the times given are corrected to holding times by subtracting the period assumed to be required to reach the correct temperature. [The times required at high temperatures are important in connexion with the sterilization of syringes on a conveyer belt by infra-red radiation, as devised by these authors (see this *Bulletin*, 1958, v. 33, 262).]

L. P. Garrod

DARMADY, E. M., HUGHES, K. E. A., JONES, J. & TUKE, W. **Sterilization by Conducted Heat.** *Lancet.* 1958, Oct. 11, 769–70, 1 fig.

This paper describes the use of the apparatus with which the experiments in the foregoing paper were done, for sterilizing instruments and syringes. The insulated aluminium block has holes bored in it to take syringes and a covered tray for instruments. Observations were made with thermocouples clipped to scissors or scalpels, held in the jaws of forceps or placed in the plungers of syringes, to determine the mode of operation required to ensure sterilization according to the standards of time and temperature previously defined. If the hot plate is at 190°C. syringes require 18 and instruments 30 minutes: starting from cold calls for 30 and 45 minutes. This apparatus is particularly convenient for the small user. *L. P. Garrod*

RICE, H. M. **Testing of Air-Filters for Hospital Sterilisers.** *Lancet.* 1958, Dec. 13, 1275–7, 6 figs.

The importance of filtering the air used to break the vacuum in dressing sterilizers has been emphasized by HOWIE & TIMBURY [this *Bulletin*, 1957, v. 32, 175] and others. This paper describes a testing device for such filters in which air is made to impinge upon a Petri dish containing sterile culture medium, as it flows from the filter at the air-inlet to the chamber. Tests were made with such a device connected to a modern high-temperature high-vacuum sterilizer, and an artificially

contaminated atmosphere was produced by shaking hospital blankets over the air-inlet during the period of vacuum release.

When no filter was used a mixed bacterial growth of about 80 colonies grew on the plate after the passage of 5 cu. ft. of air. A plug of sterile, non-absorbent cotton wool 1½ in. diameter by 4 in. long packed finger tight produced sterile plates, as did a special filter made of a folded glass-paper medium (VOKES Ltd., Guildford). The cotton wool offered considerable resistance to the flow of air and doubled the time of vacuum release—from 1½ to 3 minutes.

The author concludes that both filters tested are satisfactory, but suggests that they should be used together. The special filter would safeguard against a failure to change the cotton wool plug, while the latter would prolong the life of the former by protecting it against gross contamination. He also suggests that air sampling apparatus of the sort he describes should be used routinely with all modern sterilizers.

[This is a most timely paper. Not only does it open the way for further work on the most suitable air filters for sterilizers, but it also confirms the advice given by a number of authors that cotton wool, *properly used*, may be employed with confidence as an immediate safety measure, pending the design of the perfect air filter for this application.] *J. C. Kelsey*

MAGEE, K. C. & OAKES, H. E. **Sterilisation Procedure Examination.** *Hosp. Engineer.* London. 1958, Dec., v. 12, No. 12, 278–85, 7 figs.

The title of this paper does not do it justice, for we have a most interesting account of how a large oval disinfector of 120 cu. ft. capacity was adapted to high vacuum operation. A steam-jacketed oil-sealed 7 h.p. pump was connected to the chamber exhaust and a compensated high-vacuum gauge reading absolute pressure was fitted. The pump could produce an absolute pressure of less than 10 mm.Hg in about 5 minutes. For technical reasons the chamber could not safely be used at pressures above 20 lb. per sq. in., and so the maximum operating temperature was 126°C. Automatic control was not provided and manual operation was found to be satisfactory; the equipment was, however, under close supervision by the hospital engineers.

Tests with thermocouples in loaded drums compared high vacuum operation and the low vacuum (15 in.Hg) obtainable with a steam ejector. With high vacuum steam penetration was rapid, and a complete sterilizing cycle took about an hour, including drying. After a 12½ in.Hg vacuum penetration was slow and the complete cycle took about 2 hours. The high prevacuum not only produced a more rapid penetration by the steam, but the period of drying could be reduced to a few minutes. The success of the sterilizing procedure was checked by the use of *Bacillus stearothermophilus* spores.

In a further series of experiments it was shown that penetration was not improved when the high prevacuum was held for periods of up to 8 minutes, after it had once been drawn.

Rubber gloves were successfully sterilized by the high vacuum technique but it was found that those packed nearest the outside of the metal drums suffered most damage. This was attributed to overheating due to the heat retained by the metal, and when the gloves were wrapped in thick cotton towelling they could withstand from 5 to 16 sterilization cycles. It was considered that the towelling not only insulated the gloves from the metal but that evaporation of water from it during the drying period had a refrigerating effect.

A brief report is also given of thermocouple tests on a pharmacy sterilizer.

[Pending the provision of automatic high vacuum high temperature sterilizers it may be possible to upgrade some existing equipment and this paper provides useful information about how this may be done. It is unfortunate that it was not possible to convert this sterilizer to high temperature as well as high vacuum operation. In general the maximum size for a dressing sterilizer should be about 25 cu. ft. and it is by no means certain that experimental evidence derived from these smaller machines can always be applied to those that are so much larger. In Fig. 7 the curves up to 42 minutes have been transposed in error.]

J. C. Kelsey

BARSON, T. E., PEACOCK, F., ROBINS, E. L. & WILKINSON, G. R. **The Factors influencing Sterilisation by Low Pressure Steam. Part I. Design and Instrumentation.** *J. Pharmacy & Pharmacol.* London. 1958, Dec., v. 10, Suppl., 47T–55T., 3 figs. **Part II. The Influence of Water Content of Cotton Gowns on Equilibrium Times.** *Ibid.*, 56T–59T, 3 figs.

The first paper describes the design and instrumentation of a small experimental sterilizer (16 in. diam. by 36 in. long) for the study of the factors influencing sterilization by steam at low pressure. The quality and distribution of the steam were carefully controlled, temperatures were measured by a multipoint recording potentiometer, pressures by a specially designed transducer and steam usage by a tilting bucket device. Air was discharged by downwards displacement or by a pump drawing a vacuum down to an absolute pressure of 40 mm. Hg.

Preliminary experiments with an empty chamber, downwards displacement and a partially opened valve in the chamber drain showed that steam temperature was reached successively from above downwards, but that once equilibrium had occurred no significant difference could be shown to exist. Reducing the steam inlet from ½ in. to ⅜ in. diam. did not affect the time taken but reduction to ¼ or below prolonged it.

In further experiments the partially opened valve in the chamber drain was replaced in turn by a number of commercially available steam traps. Bellows traps, bimetallic traps and combinations of these with floats gave similar results in which the attaining of equilibrium was delayed and the temperature in the drain indicated that air was not being continuously discharged. A float trap never permitted equilibrium to be reached. When the combined float and bellows trap was modified by removing the bellows element to produce a continuously flowing by-pass satisfactory results were

obtained. A more elegant modification consisted in drilling a hole in the casting to make a permanent by-pass 0·5 sq. mm. in area and replacing the bellows.

The second paper describes the use of this equipment at a pressure of 30 lb. per sq. in. to measure the heat penetration times for a drum containing 5 surgeons' gowns. At first these were equilibrated with "normal atmospheric conditions", a relative humidity of 60–70%; steam temperature was reached in the drain within 4–7 minutes, but the times taken by the centre of the drum were variable, ranging from 23–>60 minutes. When the gowns were dried for 24 hours at 50°C. they attained steam temperature almost as rapidly as the empty chamber, but were superheated by 6°C. (11°F.). The experiment was repeated and continued until equilibrium was obtained—the centre of the gowns did not fall to steam temperature for 59 hours.

When a prevacuum of 20 in. Hg was drawn steam temperature in normally moist gowns was reached in about 20 minutes with no superheating. With a prevacuum to 40 mm. Hg absolute pressure this time was reduced to 15 minutes. Dried gowns permitted a prevacuum to 20 mm. Hg absolute pressure. Steam temperature was reached in 3 minutes, with 8 to 12°C. (17 to 21°F.) of superheat.

The authors conclude that downwards displacement will work with an efficient steam trap, but that the chamber drain temperature is an unreliable indicator of conditions in the load. They attribute the superheating of dried fabrics to the heat of rehydration of dehydrated cellulose.

[These results emphasize the complexity of the problem and the need for further experimental work. It is a pity that the pump would not draw a vacuum below 40 mm. Hg absolute, in view of the finding of KNOX and PENIKETT (this *Bulletin*, 1958, v. 33, 605) that below about that point penetration times fell steeply. We look forward to subsequent publications from these authors.] *J. C. Kelsey*

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order: General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus, Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes, Leptospira; Anaerobes; Bacillus; Others.

VELLA, E. E. **Salmonellosis in Lizards of Ghana.** *J. Roy. Army Med. Corps.* 1958, Oct., v. 104, No. 4, 236–7.

"Up to December, 1956, 183 specimens of lizard droppings were examined, and of these 40 yielded salmonellae, *i.e.*, 22 per cent.

"In 28 instances the salmonellae isolated were of known types, and these are listed below, the figure in brackets indicating the number of times the organism was isolated: *S. saint paul* (1), *S. stanleyville* (4), *S. ituri* (1), *S. newport* (2), *S. lindenburg* (2), *S. takoradi* (2), *S. canastel var.* monophasic (1), *S. london* (2), *S. seegefeld* (4), *S. rubislaw* (2), *S. alachua* (1), *S. waycross* (1) and *S. christianborg* (5).

"In addition, six types, not previously described, were isolated, and the provisional names and antigenic structure of these are given below:

S. legon	4, 12 : c; 1, 5	(1)
S. tamale	8, 20 : z_{29}; —	(1)
S. akuafo	16 : y; 1, 6	(6)
S. ghana	21 : b; 1, 6	(1)
S. kokomlemle	39 : 1, v; enx	(1)
S. teshie	47 : 1, z_{13}, z_{28}; enz_{15} ...	(1)

One salmonella remains unidentified. This had the somatic antigens 3, 10, but as motility could not be induced, flagellar antigens could not be ascertained."

MORTELMANS, J. Contribution à l'étude des salmonelloses animales au Congo belge et au Ruanda-Urundi. [**Study of *Salmonella* Strains in Animals in the Belgian Congo and Ruanda-Urundi**] *Ann. Soc. Belge de Méd. Trop.* 1958, June 30, v. 38, No. 3, 547–52. [18 refs.]

The English summary appended to the paper is as follows:—

"The author gives a survey of 220 Salmonella strains found in a 5 year period in pathological cases in domestic animals in the Belgian Congo and Ruanda-Urundi."

LE MINOR, L., RAVISSE, P. & DREAN, D. Deux nouveaux sérotypes de *Salmonella*: S. Gamaba (44 : gms) et S. Bacongo (6,7 : z36 : z42). [**Two New *Salmonella* Serotoypes: S. Gamaba and S. Bacongo**] *Ann. Inst. Pasteur.* 1958, Dec., v. 95, No. 6, 746–7.

LE MINOR, L., COURTIEU, A. L., CHARIE-MARSAINES, C. & CHASSIGNOL, S. Un nouveau sérotype de *Salmonella*: S. Irenea (17 : k : 1,5). [**A New *Salmonella* Serotype: S. Irenea**] *Ann. Inst. Pasteur.* 1958, Dec., v. 95, No. 6, 747–8.

BONNEFOI, L. A. & LE MINOR, S., with the technical collaboration of D. DREAN & C. CHARIE-MARSAINES. Activités du Centre Français des *Salmonella* de l'Institut Pasteur (2e travail) [**Activities of the French *Salmonella* Centre of the Pasteur Institute**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1958, Oct.–Nov., v. 6, No. 7, 721–30. [41 refs.]

HOPTON, J. W. **The Differential Effect of Temperature on Gas Production by a Coliform Organism.** *J. General Microbiol.* 1958, Dec., v. 19, No. 3, 507–16, 6 figs. [15 refs.]

"The influence of the temperature of incubation on the course of formic acid and gas production by cultures of a coliform organism growing in buffered and unbuffered peptone media was studied. The evidence suggests that at 30° and at 37° the onset of gas production is determined by the concentration of undissociated formic acid in the culture, but that a higher

concentration of acid is required to elicit response at 37° than at 30°. Undissociated formic acid is toxic to the organism and it appears that gas is not produced in unbuffered glucose medium at 37° because the environmental conditions do not allow elaboration of hydrogenlyase before inhibitory conditions of pH value and formate concentration are attained."

BARRY, G. T. **Detection of Sialic Acid in various *Escherichia coli* Strains and in other Species of Bacteria.** [Correspondence.] *Nature.* 1959, Jan. 10, v. 183, 117–18.

MELNYKOVYCH, G. & SNELL, E. E. **Nutritional Requirements for the Formation of Arginine Decarboxylase in *Escherichia coli*.** *J. Bacteriology.* 1958, Nov., v. 76, No. 5, 518–23, 1 fig. [13 refs.]

DRAKULIC, M. & ERRERA, M. Relations entre synthèses de protéines et d'acide désoxyribonucléique chez *E. coli*. [**Relationship between Protein Synthesis and Deoxyribonucleic Acid in *Escherichia coli***] *C.R. Soc. Biol.* 1958, v. 152, No. 7, 1208–10.

O'DONNELL, J. F., MACKAL, R. P. & EVANS, E. A., Jr. **An Analysis of the Acid-Soluble Fraction of Normal and T2r-infected Cells of *Escherichia coli*, Strain B.** *J. Biol. Chem.* 1958, Dec., v. 233, No. 6, 1523–7, 5 figs. [29 refs.]

CHATTERJEE, B. R., BANERJEE, Renuka & CHAUDHURI, S. N. **Effect of Antiserum on Bacterial Adaptation: Part III. Standardization of the Triphenyl Tetrazolium Chloride Technique and the Effect of Adenosine Triphosphate on the Adaptation of Bacteria exposed to Antiserum.** *Ann. Biochem. & Exper. Med.* 1958, v. 18, No. 4, 125–32, 4 figs.

"2:3:5-Triphenyl tetrazolium chloride has been used for measuring the adaptation of *E. coli* to lactose.

"Adenosine triphosphate added during adaptation stimulates the adaptation of *E. coli* to lactose. 2:4-Dinitrophenol does not block this effect to any great extent.

"The inhibition of adaptation in antiserum treated *E. coli* is largely counteracted by adenosine triphosphate added during adaptation."

BANERJEA, A., CHATTERJEE, D. N. & MUKHERJI, R. N. **Association of *Escherichia coli* Types with Gastro-Enteritis in Different Age Groups.** *Ann. Biochem. & Exper. Med.* Calcutta. 1958, v. 18, No. 4, 121–4. [10 refs.]

"Rectal swabs and catheter specimens of stool from cases of gastro-enteritis in different age groups occurring during the summer of 1957 in Calcutta showed the following O types of *E. coli*: 055, 026, 086, 0119, 073, 02, 04, 06, 025 and 0126. Many of the cases had *E. coli* which did not fall into any of the twenty-four O types examined. The diverse types of *E. coli* obtained point to sporadic infections from unconnected sources. The presence of known and probable pathogens in most of the adult cases examined point to some role of those organisms in the causation of the disease."

HAMON, Y., with the technical collaboration of P. DUCREST & G. BRAULT. Étude des images de sensibilité des *Escherichia coli* pathogènes pour le nourrison à diverses colicines types. Intérêt épidémiologique de cette étude. [**Study of the Pattern of Sensitivity of *E. coli* from Infantile Gastro-Enteritis to Different Colicin Types. Epidemiological Interest of this Study**] *Ann. Inst. Pasteur.* 1958, July, v. 95, No. 1, 117–21.

The English summary appended to the paper is as follows:—

"Strains belonging to the same infantile gastro-enteritis *E. coli* lysotype and possessing the same colicinogenic state have been submitted to the action of fourteen different colicins. They have presented several patterns of sensitivity to these colicins. All the strains originating from the same epidemiological focus generally possess the same pattern of sensitivity, which the author proposes to name 'colicinotype'. The determination of colicinotypes, or colicin-typing, presents a great interest for epidemiological studies; it is a complement of phage-typing, of the study of colicinogenic activity and of the identification of colicins among *E. coli* of infantile gastro-enteritis."

JACOB, F. & WOLLMAN, E. L. Sur les processus de conjugaison et de recombinaison génétique chez *Escherichia coli*. IV. Prophages inductibles et mesure des segments génétiques transférés au cours de la conjugaison. [**The Processes of Conjugation and Genetic Recombination in *Escherichia coli*. IV. Inducible Prophages and Measure of Genetic Segments Transferred during Conjugation**] *Ann. Inst. Pasteur.* 1958, Nov., v. 95, No. 5, 497–519. [19 refs.]

In crosses between HfrH and F^- *Escherichia coli* cells when the donor carries a prophage and the receptor is not lysogenic the transfer of the prophage to the receptor cell is followed by vegetative phage development and lysis of the receptor. This process is called "zygotic induction". As prophages are situated along the bacterial chromosome like any other genetic determinant, the degree of zygotic induction of different prophages is a measure of the length of the piece of chromosome which has been transferred during conjugation.

Crosses have been made between HfrH lysogenic donors and F^- non-lysogenic receptor cells, and HfrH non-lysogenic and F^- lysogenic cells, and an analysis made of the amount of zygotic induction, the frequency of recombination and the kind of recombinants obtained. In this way the position of 7 different prophages on the bacterial chromosome were localized; each occupies a definite and unique position. At the same time the transfer of genetic determinants during conjugation could be distinguished from the second stage of the process, the transmission of the determinants to the daughter cells after recombination. A comparison of the results of these reciprocal crosses provides information about the polarity of the bacterial chromosome. A map of the HfrH linkage group has been drawn, with proximal and distal ends. The further along the chromosome, the lower the frequency

of transmission of a given character, or the lower the frequency of zygotic induction of a given prophage. The gradient appears to be due to a polarity of transfer and not a gradient of integration into recombinants because the gradient observed in those crosses followed by zygotic induction (and therefore no transmission of genes to offspring) was identical with the gradient observed in the frequency of recombination in those crosses in which zygotic induction could not occur. The polarity appears to extend the whole length of the HfrH linkage group, without any break between characters transmitted with high and low frequency.

This work does not provide evidence for the hypothesis that the zygote receives the whole chromosome from the donor and that a part of it is later eliminated. The authors conclude instead that only part of the chromosome is ever transferred and that this fragment is oriented and has no fixed point of fracture.

Janice Taverne

STJERNHOLM, R. & WOOD, H. G. **Differential Degradation of D- and L-Glycerol-1-C14 by** *Aerobacter aerogenes*. *Arch. Biochemistry*. 1958, Nov., v. 78, No. 1, 28–32. [21 refs.]

OSTROM, C. A. **Studies of the Oral Flora in Experimental Airborne Infection: *Klebsiella pneumoniae* as an Indicator Organism.** *J. Infect. Dis.* 1958, July–Aug., v. 103, No. 1, 12–18, 1 fig. [Refs. in footnotes.]

Mice were exposed to aerosols of *Klebsiella pneumoniae* and at 2-hour intervals thereafter their mouths were swabbed and examined for the presence of the organism. A selective medium was used based on casamino acids and containing lactose, methylene blue, neutral red, potassium phosphate and sodium glycocholeate. The klebsiellae disappeared rapidly from the mouth after exposure and practically none were found during the first 20 hours. Then, as lesions developed in the lungs, the organisms reappeared in the mouth and continued present until death, or for at least 150–200 hours in the mice that survived. Some confusion was introduced into the counts by coprophagy, and in some experiments efforts were made to prevent this, without greatly altering the picture. *R. E. O. Williams*

ANDRÉ, J., AUDEBAUD, G. & TRAN VAN DU. Diagnostic rapide de la diphtérie par l'action sur les cellules en culture de la toxine présente sur les écouvillons de prélèvements pharygnés. [**Rapid Diagnosis of Diphtheria by means of the Cytopathogenic Effect of the Toxin Present on Throat Swabs**] *Ann. Inst. Pasteur*. 1958, Dec., v. 95, No. 6, 773–4.

The English summary appended to the paper is as follows:—

"Throat swabs from a diphtheria angina retain enough toxin to induce characteristic lesions on trypsinated monkey kidney tissue cultures.

"The early appearance of these lesions, the specificity and sensitivity of the method, suggest its use for a rapid diagnosis of the disease."

PEIZER, Lenore R., BOSSO, L. & WIDELOCK, D. **A Semi-Synthetic Autoclavable Medium for a Routine Tuberculosis Laboratory.** *Amer. Rev. Tuberculosis*. 1958, Nov., v. 78, No. 5, 788–92.

After many attempts to enrich a base medium so that it would give primary growth of tubercle bacilli the following medium was devised.

In the order as given the following reagents were dissolved in 450 ml. distilled water: sodium glutamate 40 gm., dextrose 4 gm., $Na_2HPO_4.7H_2O$ 2·9 gm., KH_2PO_4 2 gm., yeast extract (Difco) 0·2 gm., ferric ammonium citrate (USP) 0·1 gm., citric acid (USP) 0·1 gm., $Mg_2SO_4.7H_2O$ 0·1 gm., biotin 0·1% sterile solution 4 ml., Triton (WR 1339) 5% sterile solution 3 ml., glycerin (USP) 10 ml. and Starlac (an instant soluble milk product) 7 gm.

This mixture is slowly brought to the boil and 15 gm. potato starch in 82 ml. distilled water are added. Boiling is continued for about 3 minutes with stirring until the solution is clear and 1 ml. of 0·1% brilliant green, 11 gm. of molten agar in 400 ml. distilled water and sodium pyruvate 5 gm. in 50 ml. distilled water are added. The medium is distributed into 10 ml. quantities in tubes, autoclaved at 110°C. for 5 minutes, and then sloped.

Of 22,844 specimens, 1,184 were positive for tubercle bacilli on Löwenstein-Jensen medium or Peizer and Schecter medium and 1,175 were positive on the semi-synthetic medium. At the end of 6 weeks' incubation 65 cultures were positive on the egg media but negative on the new media, and the converse occurred 49 times. By 8 weeks 47 of the latter 49 cultures and 24 of the former 65 were still negative. 230 cultures on the egg media and 342 on the new medium were contaminated.

Early growth on the new medium is smooth and inclined to be mucoid, but becomes typically rough and dry later. Judging from the results on 50 strains of tubercle bacilli and 110 sputum concentrates, the medium is suitable for drug-sensitivity tests.

S. R. M. Bushby

DEKKER, T. & HUITEMA, H. **Importance of Zinc for the Growth of Surface-Culture of *Mycobacterium tuberculosis* var. *bovis* and Large-Scale Production of Tuberculin Purified Protein Derivative.** [Correspondence.] *Nature*. 1958, Nov. 15, v. 182, 1387–8.

These workers have been troubled during the last 8 years with the premature sinking of the growth during the production of tuberculin in the Dorset-Henley synthetic medium, and all their attempts to prevent this happening had failed until they tried the effects of adding zinc to the medium, as recommended by WILLISTON, BINGENHEIMER and ROSENTHAL [this *Bulletin*, 1958, v. 33, 697] the value of zinc had also been reported by LOGINOVA (*Voprosy Med. Khimii*, 1955, v. 1, 416). Addition of 10 μgm. zinc per ml., 10 μgm. zinc + 2·5 μgm. manganese per ml., or 10 μgm. zinc + 2·5 μgm. manganese + 0·35 μgm. cobalt per ml., gave excellent results.

The colour of the protein precipitate from the zinc medium was considerably whiter than from sinking

cultures, and the larger reactions in rabbits with mammalian tuberculosis, but not in guineapigs sensitized with avian strain, suggested that there was a higher proportion of the "A + B" proteins in the resulting tuberculin; chromatography confirmed this suggestion, the concentration of the "A + B" proteins being 2–3 times as high as that in the tuberculoprotein from the sinking cultures. *S. R. M. Bushby*

HAAGEN, E. & HAAGEN-CRODEL, B. Über das Verhalten von Tuberkelbazillen in der Zellkultur. **[The Behaviour of Tubercle Bacilli in Tissue Culture]** *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 7/8, 525–49, 30 figs. (1 coloured) on 6 pls. [10 refs.]

The growth of different strains and types of tubercle bacillus in a variety of tissue cultures has been investigated. The tissue culture material included cell strains obtained from mouse kidney, ox tongue, mouse skin, one derived from mouse leukaemia tissue, one from mouse sarcoma, one from pig skin and one from HeLa cells.

The medium used for the cultivation of most of these preparations was made up of horse serum and chick embryo extract and a hydrolysate of lactalbumin in a basal solution of balanced salt content, usually Earle's.

The main outcome of these observations was to establish the following points:—

Symbiosis of the cells and the bacilli appeared to be possible to a remarkable extent, the cells remaining capable of reproduction notwithstanding the heavy growth of the bacteria which appeared to be intracellular, epicellular and extracellular in varying degrees. There was never any evidence of invasion of the cell nucleus, however, and it was noteworthy that the tubercle bacillus did not appear capable of penetrating the HeLa cells. The growths were most abundant in the ox tongue culture and the speed with which growth takes place in these circumstances is emphasized in view of possible use of tissue culture methods in accelerating the bacterial diagnosis of tuberculosis.

J. W. McLeod

WILLCOX, M. C. **Simplified Sodium Hydroxide Method for the Culture of Tubercle Bacilli from Sputum.** *J. Med. Lab. Technol.* 1958, Oct., v. 15, No. 4, 269–74.

The author set out to explore the possibilities of reducing manipulation during the treatment of tuberculous sputa, and thus reduce the hazard of infection to the worker. He added 2 ml. quantities of 72 specimens of sputa to equal volumes of 4% NaOH, and after 30 minutes at 37°C. inoculated 2 slopes of Löwenstein-Jensen medium from each (Cultures A). The specimens were then centrifuged for 20 minutes at 3,000 r.p.m. and 2 slopes of the media were inoculated from the supernatant fluid (Cultures B) and 2 from the deposit (Cultures C). Stained smears were also made of the specimens before centrifuging, and of the deposits.

34 of the specimens were positive by all 3 cultures, 1 by A alone, 2 by B alone, 1 by C alone and 1 by A and B alone. In 7 specimens there was a difference between the degrees of growth in the A and C; in 2, A was better than C, and in 5, C was better than A.

33 of the specimens were positive by smear and all of these were positive by culture by all the methods. These specimens were also positive in the smear made before centrifuging and in that made from the deposit.

The contamination rate of the cultures was 3·7% but no one method had significantly more contaminated slopes than the others.

The author concludes that with smear-positive sputa there is no advantage in centrifuging (which is a dangerous procedure) but that the information from the experiments was insufficient to judge the efficiency of method A for culturing from the smear-negative sputa. The number of specimens yielding positive cultures from the supernatant fluid after centrifuging illustrates, however, the inefficiency of this method for concentrating tubercle bacilli in sputum. *S. R. M. Bushby*

KAPRAL, F. A. & STINEBRING, W. R. **The Effect of Glucose on the Tuberculin Reaction in Tissue Culture.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 712–24, 3 figs. [14 refs.]

The cells used in these cultures were monocytes derived from the peritoneal cavity of normal and BCG-immunized guineapigs, the cellular exudate being induced by the injection of liquid paraffin. The cells were transferred to a medium containing 20% normal guineapig serum, 15% of 1·4% sodium bicarbonate solution saturated with carbon dioxide and 65% Hanks solution in which the concentration of glucose was reduced to 30 mgm. per 100 ml., the minimum concentration in which the cells remain viable.

The addition of PPD to the sensitized cells caused them to become rounded in 24–36 hours, their cytoplasm to become much more vacuolated than that of normal cells, and their phagocytic activity to decrease, shown by their failure to ingest the other leukocytes surviving in the culture; within a few days the cytoplasmic vacuoles coalesced and the cells floated off the glass. These changes could be produced by 1 μgm. per ml. but the maximum effect was produced by 5 μgm. per ml. although 10–50 μgm. per ml. accelerated the changes; cells from unsensitized animals were unaffected by 100 μgm. per ml.

The utilization of additional glucose (250 μgm. per ml.) by sensitized and unsensitized cells was unaffected by the addition of PPD but the injury to the sensitized cells by PPD was delayed. In the experiments with low concentrations of glucose the cells lost their ability to respond to the PPD when its addition was delayed, and in the different experiments this occurred with intervals ranging from 2 to 6 days; with the high concentration of glucose the injury, instead of appearing in 24–36 hours after the addition of the PPD, appeared in 2–10 days in different experiments and the time over which the cells remained susceptible to PPD was lengthened.

These results conflict with the findings of some other workers [this *Bulletin*, 1936, v. 11, 941; 1954, v. 29, 204] and some possible explanations are discussed.

S. R. M. Bushby

GREENBERG, L., EIDUS, L. & DIENA, B. B. **The Vital Staining Method for the Rapid Estimation of the Bacterial Count of BCG Vaccine.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 785–7.

In this method 15 mgm. of the BCG vaccine are inoculated into 4·5 ml. of Sauton medium and grown for 24 hours; 0·25 ml. of 1% neotetrazolium chloride is then added. After 48 hours' incubation a 1 : 50 dilution is prepared in Erlenmeyer flasks containing steel balls. After shaking, 0·1 ml. is placed in 6 mm. bottomless cups fixed by means of nail varnish to glass slides. After drying at 56°C. the cup is removed and the proportion of bacilli staining purple with the reduced dye is counted; the inactive cells are made visible with picric acid or other yellow staining substance.

In the examination of 83 vaccines by this method, excellent agreement was found between the plate counts in 49 of 56 vaccines prepared by the classical method and harvested on the 14th day, in 17 of 20 vaccines harvested before the 11th day, and in all of 7 freeze-dried vaccines. A difference was noted between the vaccines harvested on the 14th day and those harvested earlier than the 11th day; with the former the standard plate count paralleled the microscopic-cell-plus-clump count whereas with the latter it paralleled the microscopic individual count.

Thus, in this method, which is rapid (2–3 days), good agreement was found in 90% of the vaccines and the differences observed in the others were no greater than those which have been observed at times between replicate plate counts. *S. R. M. Bushby*

MILLMAN, I. **Formation of Protoplasts from Mycobacteria by Mycobacteriophage.** *Proc. Soc. Exper. Biol. & Med.* 1958, Oct., v. 99, No. 1, 216–9, 6 figs.

This report describes the successful use of mycobacteriophage for converting tubercle bacilli to protoplasts. This change was accomplished by adding concentrated phage in the proportion of 1,000 particles to each bacillus in 10% sucrose plus 0·1% $MgSO_4$ and incubating for 1 hour. Light microscopy and electron microscopy showed that by 15 minutes the bacilli were markedly swollen and that by the end of the hour complete protoplasting had occurred.

Strains 607, H37Rv and BCG were converted to protoplasts with the same strain of phage, although initially plaques were produced only with 607 and the phage had to be adapted by serial passage before it affected the other strains of tubercle bacilli.

S. R. M. Bushby

BRAUN, H. & LEBEK, G. Zur Biologie des Typus humanus und bovinus des *Mycobacterium tuberculosis.* [**The Biology of Human and Bovine Types of** *Myco. tuberculosis*] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 7/8, 519–24, 2 figs.

Working with 215 human and 150 bovine strains of the *Myco. tuberculosis* collected in the Ludolph-Brauer Institute in Munich, and testing the ability of these to grow on defined media of graded nutrient content, the authors establish that the bovine type is much more exacting than the human.

The series was composed of media, all of which contained Na_2SO_4, $MgCl_2$ and potassium phosphate buffer.

In No. I the nutriment was provided by ammonium chloride and glycerin; No. II had also one amino acid, asparagin; No. III contained the same salts with a mixture of amino acids and No. IV was as No. III with addition of serum.

Of the human strains 96·74% grew in No. I, 2·79% in No. II and 0·47% in No. III; whereas of the bovine strains only 0·66% grew in No. I, while 12·67% grew in No. II, 22·67% in No. III and, the rest, 64% in No. IV.

Hence the value of adding serum to much used medium, such as Löwenstein-Jensen, and the high value of Tarshis medium which contains 30% of human blood [this *Bulletin*, 1953, v. 28, 1095]. *J. W. McLeod*

LYON, R. H., LICHSTEIN, H. C. & HALL, W. H. **Influence of Age on Metabolic Activity of** *Mycobacterium tuberculosis. Proc. Soc. Exper. Biol & Med.* 1958, Oct., v. 99, No. 1, 79–81, 3 figs.

H37Ra was grown in Sauton medium plus 0·02% Tween 80; the bacilli were collected by centrifuging, washed twice in distilled water and suspended in phosphate buffer. Their lactate oxidation was measured in the Warburg apparatus.

Preliminary studies showed that the optimum *p*H range was 5·9–6·6 with maximum activity at *p*H 6·4, and the optimum concentration of lactic acid for the 10–12 mgm. inoculum was between 1·66 and 2·32 × 10^{-2} M.

For determining the effects of the age of the culture on the lactic acid oxidation, the bacilli were harvested at intervals between the 4th and 20th days of incubation. Maximum oxidation occurred between the 10th and 12th days, the QO_2 being approximately 6·2 at the 4th day, about 7·5 at the 8th to 12th days, 6·5 at the 13th day, and 6·0 by the 20th day. Maximum oxidation of the substrate was therefore observed during the logarithmic phase of growth and the authors suggest that young cells should be more widely used in studies of the physiology of the tubercle bacillus.

S. R. M. Bushby

SCHWEIGER, O. & VANDRA, Edit. **Bacteriologic and Clinical Significance of the Catalase Activity of** *Mycobacterium tuberculosis. Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 735–48, 2 figs. [24 refs.]

This report comes from the National Institute of Tuberculosis, Koranyi, Budapest. Sputum from 20 patients with advanced cavitary tuberculosis, who had had long courses of isoniazid, was cultured on Löwenstein-Jensen medium with and without 10 μgm. isoniazid per ml. Sensitive bacilli were eliminated from those growing on the isoniazid-containing medium by subculturing twice on to the same medium, and the bacilli from both cultures were then examined for isoniazid sensitivity, catalase production, cytochemical tests of DUBOS, DESBORDES and WILSON, and virulence for guineapigs.

Usually abundant growth was seen in 4–6 weeks on the isoniazid-free medium and in 8 weeks or longer on

the isoniazid-containing medium. From only 3 of the patients were susceptible bacilli grown but resistant bacilli were also isolated from these patients. Marked differences were found in the results of cytochemical tests and no correlation was found between these and the results of the virulence tests or the degree of isoniazid-resistance and catalase activity. The degree of isoniazid-resistance varied greatly not only from patient to patient but within the same patient on different occasions.

The 3 isoniazid-sensitive strains were catalase-positive and virulent to guineapigs and all the strains resistant to 80 μgm. isoniazid per ml. were catalase-negative and of low virulence. Strains resistant to 5–10 μgm. per ml. were equally catalase-positive and -negative but those resistant to 20–40 gm. per ml. were mainly catalase-negative; although the majority of the strains were of low virulence, most of the catalase-positive strains were virulent.

Catalase activity at *p*H 1·0 and *p*H 7·0 was also compared; 2 of the 14 strains that were catalase-positive at both reactions showed decreased virulence but in contrast 5 of the 9 strains which were negative at *p*H 1·0 showed decreased virulence. Both catalase activity and degree of virulence varied in the strains isolated on different occasions from the same patients.

An attempt was made to relate these findings with the course of the disease, but 7 patients had to be excluded because positive cultures were not obtained in each test. The patients were divided into 2 groups; those with continuously good clinical states in spite of persisting cavities and continuously positive sputa, and those with clinically progressive disease; 3 of the latter group died. Isoniazid-sensitive bacilli were isolated from 1 of the first group and from 2 of the second group, but otherwise no difference in the degree of resistance was found in the bacilli of the groups. In contrast, however, from the 6 patients in the good clinical state, catalase-positive strains were isolated on 5 occasions and catalase-negative strains on 23 occasions, whereas from the other group catalase-positive strains were isolated on 11 occasions and catalase-negative on 8 occasions; the incidence of virulent strains in the 2 groups was similar to that of the catalase-positive strains.

Thus, in general, there was some degree of relationship between the bacteriological findings and the clinical course of the disease, catalase-negative strains being found more frequently in patients in whom it was favourable. Although the bacterial populations of tuberculous patients are far from homogeneous, it would seem that serial catalase and virulence tests are of value in assessing prognosis. The authors conclude by emphasizing that catalase-negative strains should not be considered as harmless to man. *S. R. M. Bushby*

VANDIVIERE, H. M., MELVIN, Irene G. & KENNEDY, H. E. **Titration of Cord Formation as a Measure of Pathogenicity of Wild-Type Acid-Fast Bacilli, Typical and Atypical.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 799–801, 1 fig.

To test further the validity of the cord-titration method [this *Bulletin*, 1959, v. 34, 162] for assessing virulence, the authors have made an extensive study of 33 wild type strains of mycobacteria; 21 of these strains were typical rough strains of tubercle bacilli from patients with tuberculosis, 2 were smooth strains and 10 were "atypical" strains. H37Rv and a strain of *Mycobacterium phlei* were included in the examination. The examination consisted of colony appearances, isoniazid sensitivity, catalase activity, cord titre and Feldman's index of virulence in guineapigs.

Except for the 2 smooth strains which did not form cords but produced a mean Feldman's index of 45, the strains of tubercle bacilli that showed high virulence gave high cord titres (over 0·1). The "atypical" strains were avirulent or only slightly virulent and produced low cord titres. With the isoniazid-resistant, catalase-negative strains the variation with cord titre was not significant and although the Feldman index was low, it was still higher than that of the "atypical" strains.

Thus, a general correlation was found between cord titre and virulence for the guineapig with rough wild strains, but the authors emphasize that for the cord titres of other workers to be comparable, the authors' technique must be closely adhered to.

S. R. M. Bushby

YOUATT, Jean. **The Uptake of Isoniazid by washed Cell Suspensions of *Mycobacteria* and Other Organisms.** *Australian J. Exper. Biol. & Med. Sci.* 1958, June, v. 36, Pt. 3, 223–33, 8 figs. [10 refs.]

In these experiments washed suspensions of the organisms were suspended in the required medium containing radio-active isoniazid in Warburg manometer flasks and shaken at 120 strokes per minute. At the desired time a sample was removed, the bacteria were washed and collected by centrifuging and their radioactivity measured.

The uptake from a saline solution of 50 μgm. isoniazid per ml. by isoniazid-sensitive BCG was linear with time at temperatures 18° and 28°C. but became progressively less at 37°C. although it was approximately linear during the first hour. Heat-killed bacilli also took up isoniazid, the uptake being approximately 20% of that of the viable bacilli. With higher concentrations of the drug the uptakes of both living and dead bacilli increased but not in direct proportion to the increase in concentration. The presence of oxidizable substrates, *e.g.* glucose or glycerol, depressed the uptake but stimulated respiration. The rate of uptake by living but not dead bacilli was increased by aeration, especially with oxygen; under anaerobic conditions the uptake was very small.

The uptake of isoniazid therefore appears to be due to 2 processes; in one it is metabolic, and for this energy is required, and in the other it is non-metabolic, and this appears to be due to diffusion. Chemical inhibition such as that due to sodium cyanide, potassium fluoride and sodium azide depressed the uptake, but 2,4-dinitrophenol had a stimulating effect at first, followed by a depressing effect. Variation in *p*H between 6 and 8 had little effect. Previous exposure of the bacilli to such chelating agents as o-phenanthroline or ethylene diamine tetra-acetate had no effect on the uptake.

The uptake of isoniazid by bacteria of other genera was very small and this is consistent with the view that the uptake of this drug by insensitive organisms is negligible. Isoniazid-resistant BCG behaved similarly except when exposed to CO_2; under this condition the uptake became comparable to that of sensitive bacilli, a change which seems to be due to an increase in permeability.

The presence of pyridoxal in concentrations from 5 to 50 μgm. per ml. increased the uptake and this effect was seen with both living and dead cells. Pyridoxal *iso*-nicotinoyl hydrazone was taken up readily by both living and dead bacilli, which suggests that the stimulating effect of pyridoxal is due to the formation of the hydrazone. *S. R. M. Bushby*

YOUATT, Jean. **Metabolism of Isoniazid by *Mycobacterium tuberculosis* BCG with reference to Current Theories of the Mode of Action.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 806–9, 1 fig.

KRÜGER-THIEMER (*Amer. Rev. Tuberculosis,* 1958, v. 77, 364) has suggested that organs susceptible to isoniazid do not take up isonicotinic acid and that, when isonicotinic acid is formed in the cells, it accumulates and disturbs the normal metabolism by competing with nicotinic acid. The work described in the present paper is considered to be highly relevant to this theory.

In these experiments, BCG and an isoniazid-resistant variant of the bacillus were suspended in a phosphate buffer *p*H 7 containing radio-active isoniazid and at varying periods the residual drug, the isonicotinic acid formed and the concentration bound within the cells were determined. The results with living and dead BCG show that isonicotinic acid is formed in the cells, but that the acid is found in the suspending medium in concentrations which approximate closely to the theoretical yields from the isoniazid lost and that there is no apparent lag between the disappearance of the drug and the appearance of the acid. This is interpreted as showing that the acid leaves the cell readily and is therefore not in agreement with the theory that the action of isoniazid involves the accumulation of the acid within the cell. In these experiments, breakdown to isonicotinic acid also occurred with dead cells but at a much slower rate.

In experiments in which the sensitive and the resistant bacilli were shaken with radio-active isoniazid and isonicotinic acid, the resistant bacilli took up only about 20% as much isoniazid as did the sensitive bacilli, although they took up the acid at about the same rate as the sensitive bacilli.

Thus these results fail to support the hypothesis that isoniazid intoxication is due to its breakdown to isonicotinic acid, and the author has been unable to obtain any evidence to support the theory that isoniazid acts by chelating or that it inhibits transaminase systems. The author acknowledges that it is easier to discard theories than to replace them, but he hopes that the observation that isoniazid-sensitive tubercle bacilli growing in the presence of isoniazid produce a yellow pigment may supply a clue to the mode of action of the drug. This pigment is produced only in the presence of aeration; its production is unaffected by iron salts or chelators but it is inhibited by NaCN and NaN_3; its production appears to be specific to isoniazid. Paper chromatography suggests that it is not homogenous but as it is unstable this may be due to breakdown products. Spectrographically it has one peak between 300 and 700 μ, maximum absorption being at 450–460 μ. Its fluorescent properties are similar to those of flavines so it is tempting to suggest that it is the result of altered flavine synthesis but there are not sufficient data to warrant this conclusion.

S. R. M. Bushby

URBANCÍK, R. **Bacteriotropic Activity of Isoniazid in the presence of Certain Other Compounds.** *Amer. Rev. Tuberculosis.* 1958, Nov., v. 78, No. 5, 802–5.

PAB and some other arylamines have been shown to increase the antituberculous *in vitro* activity of isoniazid. In the present paper, 100 μgm. tryptophan per ml. and 50 μgm. indole per ml. in Youmans medium decreased the minimum inhibitory concentration of isoniazid from 10 μgm. per ml. to 5 μgm. per ml., and 100 μgm. uric acid per ml. increased the minimum inhibitory concentration to over 25 μgm. per ml. The following substances had no effect on the activity:—anaesthesine, procaine, tetracaine, folic acid, anthranilic acid, sulphanilic acid, *p*-oxybenzoic acid, sulphanilamide and methionine.

In a second experiment in Long medium, the increased activity of isoniazid in the presence of PAB, indole and tryptophan was confirmed by determining the weights of growth of H37Rv and of a photochromogen in the presence of 0·05 μgm. isoniazid per ml. with and without these enhancing substances. In this experiment, uric acid was shown to increase the amounts of growth. Of especial interest was the red pigmented growth of H37Rv in the presence of indole whereas the pigment of the photochromogen was only slightly increased.

The author concludes from these results that for this enhancement either a carboxyl or a free amino group is necessary, and that the *para* configuration seems to be of equal importance. *S. R. M. Bushby*

LUTZ, A. & WITZ, M. A. Effet thérapeutique de l'association isoniazide-streptovaricine sur la tuberculose expérimentale du cobaye. [**Therapeutic Effect of the Isoniazid-Streptovaricin Association on Experimental Tuberculosis in Guineapigs**] *Ann. Inst. Pasteur.* 1958, Nov., v. 95, No. 5, 529–33, 2 figs.

45 guineapigs were infected subcutaneously with 1 ml. of a mixture of equal parts of a 1:10 dilution of Dubos cultures of H37Rv and an isoniazid-resistant strain of tubercle bacilli; both of these strains were sensitive to streptovaricin, the inhibitory concentrations being 0·1 and 0·04 μgm. per ml. respectively. On the 24th day of infection, 6 of the animals were killed and the others were divided into 4 groups, one group being treated with 1·7 mgm. isoniazid per kgm. orally per day, another

with 20 mgm. streptovaricin per kgm. orally per day, and a third group with these doses of the 2 drugs together. The fourth was a control group. On the 84th day the surviving animals were killed and the degree of tuberculosis was assessed by the method of Feldman and Hinshaw.

100% of the control animals died and these had a tuberculosis score of 87·2 as compared with 68·5 for the pretreatment controls. 100% of the animals treated with streptovaricin alone died and their score was 67·3, whereas 100% of the animals treated with isoniazid alone survived and their score was 21·4, and 90% of the animals on the combined therapy survived and their score was 4·4; the 10% of animals of this latter group which died had a score of 12.

Cultures from the spleens and lungs of 3 of the combined-treatment group grew no tubercle bacilli whereas cultures from both the spleens and 1 of the lungs of 2 of the isoniazid group grew a few tubercle bacilli; tubercle bacilli were grown from the livers of both groups but they were more numerous from the isoniazid group.

Combined therapy with these sub-optimal doses of isoniazid and streptovaricin has therefore shown a synergic action in this mixed infection.

[See also this *Bulletin*, 1958, v. 33, 696.]

S. R. M. Bushby

LIBERMANN, C. Étude de quelques souches de *Mycobacterium tuberculosis* isoniazido-résistantes et fortement pathogènes pour le cobaye. Deuxième Mémoire. Discussion des résultats. [**Study of some Isoniazido-Resistant Strains of** *Mycobacterium tuberculosis* **Highly Pathogenic for Guineapigs. II. Discussion of the Findings**] *Ann. Inst. Pasteur.* 1958, Oct., v. 95, No. 4, 432–48, 8 figs. [15 refs.]

The strains examined were the 4 on which previous pathogenicity studies have been reported [this *Bulletin*, 1958, v. 33, 695].

Because of the difficulty of expressing the precise sensitivity to isoniazid, the author determined the 50% lethal dose (LD50). This was calculated graphically on probit logarithmic paper after determination of the minimum concentration of isoniazid which inhibits either all or all except a few of the bacilli of a constant inoculum on Löwenstein-Jensen medium, and the maximum concentration which permits growth comparable to that on a control tube of the medium.

The pathogenicity of the strains was assessed by comparing the minimum lethal doses for guineapigs, the time taken to kill the animals and the severity of the lesions.

The LD50 dose of isoniazid for the DEM strain was determined 23 times, before and after passage through guineapigs and on media containing isoniazid; the mean concentration was 1·14 μgm. per ml. (5% confidence limits being 1·06–1·21 μgm. per ml.). The strain was highly virulent, 10^{-5} mgm. being lethal, and the lesions were mainly fibrofollicular. The mean LD50 dose of isoniazid for strain TIL 11 was 3·23 μgm. per ml. but the variations within the 34 experiments were from 0·45–29 μgm. per ml. (95%). The virulence of this strain was similar to that of the DEM strain but the microscopic appearance of the lesions was very variable, sometimes being typically follicular but at other times they were atypical.

The mean LD50 dose of isoniazid for strain BR1, based on 5 titrations, was 0·12 μgm. per ml. (5% confidence limits being 0·10–0·14 μgm. per ml.). No information is given on the virulence of this strain, except that the lesions it produced were mainly exudative and deaths were mainly due to their secondary effects. The LD50 dose of isoniazid for strain GO, calculated from 4 titrations, was 1·3 μgm. per ml.; this strain was of variable but low virulence.

In an attempt to assess the ability of isoniazid-resistant strains to produce tuberculosis with cavity formation, the author has examined animals infected with isoniazid-resistant strains. He found 42 with cavity formation either in the lungs, liver or spleen, and from 23 of these, cultures were made from the cavities and the organisms isolated were tested for isoniazid sensitivity; from only 4 were isoniazid-sensitive strains recovered. From his own observations and from those of others, he argues that strains of reduced virulence, which include isoniazid-resistant strains, are more likely to produce cavity formation than fully virulent strains.

The conclusions from these studies are that the TIL 11 strain produces cavities with about the same frequency as H37Rv and appears to be of equal virulence; strains BR1 and DEM also appear to be of normal virulence by these criteria. *S. R. M. Bushby*

VIALLIER, J. & CAYRÉ, R. M. Sur l'activité bactéricide de la cyclosérine vis-à-vis de *Mycobacterium tuberculosis*. [**Bactericidal Activity of Cycloserine on** *Myco. tuberculosis*] *C.R. Soc. Biol.* 1958, v. 152, No. 4, 637.

Tubes of Youmans medium plus horse serum containing cycloserine in concentrations of 12·5, 25 and 50 μgm. per ml. were inoculated with an equal number of tubercle bacilli of 10 human strains, and were incubated for 50 days. At intervals a portion of the growth was removed, centrifuged and inoculated on Löwenstein medium, which was incubated for 60 days. The sub-culture of each of the strains from the tube containing 50 μgm. cycloserine per ml. remained sterile or grew only a few colonies of the bacilli.

In further experiments with 4 of the strains, in which the antibiotic-containing cultures were incubated either at room temperature or at 4°C., the bacilli were not killed, thus showing that cycloserine is bactericidal only for actively multiplying bacilli. *S. R. M. Bushby*

VIALLIER, J. & CAYRÉ, R. M. Bacilles tuberculeux résistants à la cyclosérine. [**Tubercle Bacilli Resistant to Cycloserine**] *C.R. Soc. Biol.* 1958, v. 152, No. 5, 776–7.

Of 728 strains of tubercle bacilli from sputa or stomach washings, 684 were sensitive to 25 μgm. cycloserine per ml., 39 were resistant to 25–50 μgm. per ml. and 5 were resistant to more than 50 μgm. per ml.; 1 of the strains resistant to 25–50 μgm. per ml. was

from a patient who had not been treated with cycloserine. 1 of the strains resistant to over 50 μgm. per ml. was from a patient who had been treated with 50 gm. cycloserine, 2 others were from patients treated with 100 gm. and another was from a patient treated with 300 gm. 1 of the strains resistant to 25–50 μgm. per ml. was from a patient given about 30 gm., 9 were from patients given 50 gm., 12 were from patients given 100 gm., 3 were from patients given 200 gm. and 1 was from a patient given 300 gm.

Further studies were made of 20 of the strains resistant to 25–50 μgm. per ml.; 12 of the strains which had grown in the presence of 25 μgm. per ml. were also resistant to 1–20 μgm. isoniazid per ml. and 6–10 μgm. streptomycin per ml. All the strains produced tuberculosis in guineapigs but those resistant to isoniazid were less virulent. 11 of the strains were recovered from the guineapigs and their sensitivity to cycloserine was unaltered except for 2 which were resistant to 20–25 μgm. per ml.

[The authors use both the words *sensible* and *résistante* to apply to one group of organisms discussed, and it is difficult to follow their meaning.]

S. R. M. Bushby

Steenken, W., Jr., Montalbine, V., Smith, M. M. & Wolinsky, E. **Antituberculous Activity of Thiocarbanidin *in vitro* and in the Experimental Animal.** *Amer. Rev. Tuberculosis.* 1958, Oct., v. 78, No. 4, 570–75.

Thiocarbanidin (4-isobutyl-4′-(2-pyridyl)thiocarbanilide), in the concentration of 0·5 μgm./ml. but not at 0·1 μgm./ml., inhibited the growth in Dubos medium of H37Rv and 2 of its variants resistant to isoniazid and PAS, respectively, and of 4 recently isolated strains of tubercle bacilli; an H37Rv variant resistant to thiosemicarbazone was resistant to 50 μgm. per ml. and 4 photochromogenic mycobacteria were resistant to 0·1–0·25 μgm. per ml. but not to 1·0 μgm. per ml.

In groups of 10 guineapigs, infected intracardially with 0·1 mgm. H37Rv and in which the average survival time of the untreated animals was 33 days, 50 mgm. thiocarbanidin per kgm. given orally each day for 150 days prolonged the average survival time 4 times, and 20 mgm. streptomycin per kgm. and 10 mgm. isoniazid per kgm. prolonged it 5 and 8 times, respectively. When this dose of thiocarbanidin was given in conjunction with streptomycin and isoniazid in the same doses as when given alone, the average survival times were 7 and 9 times that of the untreated animals. In an infection by a variant of H37Rv resistant to 5 μgm. thiocarbanidin per ml., thiocarbanidin afforded no protection.

In groups of 3 rabbits each, infected intravenously with H37Rv and in which treatment with 10, 20, 40 and 80 mgm. thiocarbanidin per kgm. daily was delayed until radiograms showed the miliary stage of the disease to be well advanced, marked clearing of the disease occurred in 6 of 12 rabbits, but PAS (100, 400 and 800 mgm. per kgm.) had no effect. In an experiment in guineapigs, in which groups of 10 animals each were treated with doses of thiocarbanidin ranging from 10 to 80 mgm. per kgm. and PAS from 100 to 800 mgm. per kgm. per day for 66 days, a dose of thiocarbanidin about one-tenth that of the PAS produced comparable effects as judged by the extent of the disease 130 days from the day of infection.

In normal rabbits 10 to 80 mgm. thiocarbanidin per kgm. daily for 194 days or in guineapigs for 150 days produced no gross toxic changes. *S. R. M. Bushby*

Kuzniecow, A. Liofilizowana szczepionka przeciwgruzlicza sporządzona z prątków BCG wrażliwych i oporynch na streptomycyne w doświadczeniu na zwierzetach laboratoryjnych. [**Lyophilized Anti-Tuberculosis Vaccine prepared from Streptomycin Sensitive and Resistant BCG Bacilli, in Experiments on Laboratory Animals**] *Med. Dośw. i Mikrob.* Warsaw. 1958, v. 10, No. 4, 441–67. [61 refs.]

The English summary appended to the paper is as follows:—

"The investigations concerned lyophilized vaccine prepared from two BCG strains (French and Brazilian), streptomycin-sensitive and -resistant ones. The investigations were intended as a comparative study of the immunogenic action of the vaccines on laboratory animals (guinea pigs and white mice), and covered also the effects of streptomycin on postvaccinal resistance to tuberculosis, and dynamics of accumulation of specific haemagglutinins. Attention was also devoted to possible treatment of tuberculosis with streptomycin, combined with immunization by vaccines prepared from streptomycin-resistant BCG strains.

"The following was revealed by the investigations:

"1. Suitable adaptation affords BCG strains highly resistant to streptomycin.

"2. The lyophilized vaccine, given subcutaneously or intracutaneously to guinea pigs, causes appearance in the serum of haemagglutinins detectable with the aid of red cells sensitized with tuberculin.

"3. Lyophilized vaccines obtained from streptomycin-sensitive and resistant BCG strains have almost identical effects on the dynamics of the increase or reduction of haemagglutinins in guinea pigs. The titre of haemagglutinins and the time depend on the dosage and number of vaccinations.

"4. Intracutaneous vaccination of guinea pigs with the lyophilized BCG vaccine stimulates the production of haemagglutinins more powerfully than subcutaneous administration. Intracutaneous administration of 0·2 mg of BCG bacilli was equivalent to 5 mg. given subcutaneously, as regards production of haemagglutinins.

"5. Administration of streptomycin to guinea pigs immunized with a lyophilized vaccine prepared from streptomycin-sensitive strains reduced the haemagglutination titre from 1:64—1:128 to 1:4—1:8, unlike in guinea pigs immunized with BCG strains resistant to the drug.

"6. In experiments on guinea pigs and white mice, no essential differences in immunizing effects were revealed between lyophilized vaccines obtained from streptomycin-sensitive and -resistant BCG strains.

"7. Streptomycin did not inhibit in guinea pigs the

immunizing effects of lyophilized vaccine prepared from BCG strains resistant in varying degrees to the drug, but it did in guinea pigs immunized with analogical vaccines from streptomycin-sensitive strains.

"8. Sub- or intracutaneous 6-fold vaccination of guinea pigs, and 3-fold intraperitoneal vaccination of white mice, with a lyophilized vaccine prepared from streptomycin-sensitive and -resistant strains, prevented the development of tuberculosis in half of the guinea pigs and $\frac{1}{3}$ of the mice, and conspicuously extended the time of survival of animals infected with large doses of virulent tuberculosis bacilli.

"9. Daily 400 mcg. doses of streptomycin given to mice vaccinated 3 times intraperitoneally with the lyophilized BCG vaccine and inoculated simultaneously intravenously with a large dose of virulent bacilli, protected the animals against tuberculosis, but only when the vaccine used was prepared from streptomycin-resistant BCG strains; on the other hand the majority ($\frac{3}{4}$) of the mice vaccinated with streptomycin-sensitive BCG strains usually died within 72 days, exhibiting extensive tuberculotic changes in inner organs."

COHN, M. L., DAVIS, C. L. & MIDDLEBROOK, G. **Airborne Immunization against Tuberculosis.** *Science.* 1958, Nov. 21, v. 128, 1282–3.

The apparatus and techniques used in these experiments were those previously reported [*Amer. Rev. Tuberculosis,* 1957, v. 75, 656; this *Bulletin,* 1957, v. 32, (804)], and under the conditions that they were used in these experiments, 30 minutes' exposure of guineapigs to 1,000 well dispersed viable units of virulent tubercle bacilli per ml. of nebulizer fluid yielded approximately 1 infecting unit per guineapig. In the experiment with a freeze-dried commercial BCG vaccine, groups of 6 guineapigs were exposed to $2{\cdot}5 \times 10^4$, $2{\cdot}5 \times 10^5$ and $2{\cdot}5 \times 10^6$ viable units per ml. of nebulizer fluid for 30 minutes. and then tested with 300 tuberculin units 41 days later. On the 70th day the animals were challenged by the same route with H37Rv, and 28 days later viable counts were made of the tubercle bacilli in homogenates of the spleen and lungs.

The results showed that all but 2 of the animals exposed to the lower concentration of BCG became tuberculin-positive and that there was a significant difference ($p < 0{\cdot}001$) between the number of bacilli in the tissues of the tuberculin-positive animals and the tuberculin-negative ones, which included 6 control unimmunized animals; the differences in the bacterial counts were greater than 100-fold. The only effect of increasing the immunizing dose of BCG appeared to be an increase in the percentage of animals becoming tuberculin-positive. This particular vaccine was poorly dispersed, and many of the bacterial units were too large to be inhaled, but with a better dispersion fewer than 25 infective units per animal would probably give significant immunity.

Except for slight enlargement of the mediastinal glands, which contained a few collections of epithelioid cells, harbouring small numbers of bacilli, no abnormalities were found in guineapigs 35 days after exposure to the BCG. That multiplication of the bacilli is necessary for the development of the immunity was shown by immunity failing to develop when isoniazid was given for 10 days after exposure to the BCG.

Similar protection was given by a strain of BCG that had been kept for long periods in deep-freeze, but not by another strain which had been grown frequently in Tween-albumin medium.

As the authors had frequently noted a loss of infectivity of strains of tubercle bacilli grown repeatedly in Tween-albumin medium, they maintain that the airborne infection route provides a quantitative means of defining infectivity of attenuated strains of tubercle bacilli, and in their opinion the implications of the results of these experiments are that inhalation of BCG should be tried in man, and that immunization by the same route should be tried in animals against other respiratory tract infections with attenuated parasites.

S. R. M. Bushby

HALPERN, B. N., BIOZZI, G., STIFFEL, C. & MOUTON, D. Corrélation entre l'activité phagocytaire du système réticulo-endothélial et la production d'anticorps antibactériens. [**Correlation between the Phagocytic Activity of the Reticulo-Endothelial System and the Production of Antibodies to Bacteria**] *C.R. Soc. Biol.* 1958, v. 152, No. 5, 758–61, 1 fig.

Mice given BCG showed an increased phagocytic activity of the reticulo-endothelial system and enlargement of the liver and spleen. When inoculated with a heat-killed suspension of *Salmonella typhi* these animals give much higher titres of O and H antibodies than untreated controls. These results agree with work of DUBOS and SCHAEDLER [this *Bulletin,* 1958, v. 33, 270], who found an increased resistance to staphylococcal infection in animals which had received BCG.

Sheila McDonald

BERGEL, M. Primera lepromina animal con bacilos de Hansen: obtención y estudio comparativo con leprominas humanas. [**First Animal Lepromin with Hansen's Bacillus: its Preparation and Comparative Study along with Human Lepromins**] *Semana Méd.* 1958, Aug. 7, v. 113, No. 6, 271–80, 292, 24 figs. English summary.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 449.]

HANKS, J. H. **The Magnitude of the Immune Response incited by Killed and Attenuated Mycobacteria.** *J. Immunology.* 1958, Oct., v. 81, No. 4, 297–301, 2 figs. [12 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 456.]

OLMOS CASTRO, N. & ARCURI, P. B. **Attempts to obtain an Antigen (LPT) suitable for Study of Hypersensitivity in Leprosy.** *Internat. J. Leprosy.* New Orleans. 1958, Jan.–Mar., v. 26, No. 1, 51–6.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 450.]

YAMAMOTO, T., NISHIURA, M., HARADA, N. & IMAEDA, T. **Electron Microscopy of Ultra-Thin Sections of Lepra Cells and** *Mycobacterium leprae*. *Internat. J. Leprosy*. New Orleans. 1958, Jan.–Mar., v. 26, No. 1, 1–8, 1 text fig. & 13 figs. on 9 pls. [17 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 447.]

PÖHN, H. P. Zur Differenzierung von Staphylokokken. [**The Differentation of Staphylococci**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, July–Aug., v. 116, Nos. 1/2, 92–108. [Numerous refs.]

This paper offers a competent review of the various tests that have been used to recognize pathogenic staphylococci and to subdivide the species into types for epidemiological purposes. It cannot conveniently be abstracted. *R. E. O. Williams*

SEDLÁK, J. & PRUCHOVÁ, Jaroslava. Zur Laboratoriumsdiagnostik von Enterotoxicosis staphylococcica. [**The Laboratory Detection of Staphylococcal Enterotoxin**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, July–Aug., v. 116, Nos. 1/2, 109–25, 6 figs. [59 refs.]

The authors briefly review the testing of staphylococci for their ability to produce enterotoxin. Although the feeding of human volunteers is the most reliable method, it is not often practicable. None of the established animal tests is regarded as really useful for routine work. A few tests of culture filtrates on isolated rat duodenum are reported, and this method is considered satisfactory. [But *cf.* KELSEY & HOBBS and ANDERSON, JAMES & MARKS, this *Bulletin*, 1955, v. 30, 360 for a report of a test of rabbit gut. Clearly more work would be needed before the rat-gut test could be accepted.] *R. E. O. Williams*

GRÜN, L. Über ein neues Staphylokokken-Antigen. [**A New Staphylococcal Antigen**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 3, 259–62.

The new antigen, *l*, is an addition to OEDING's series and was first recognized in a strain from raw milk. It is thermolabile and can exist in a blocked form, but can be identified in young or in autoclaved cultures. *R. E. O. Williams*

DISALVO, J. W. **Desoxyribonuclease and Coagulase Activity of Micrococci.** *Med. Technicians Bull. Suppl. to U.S. Armed Forces Med. J.* 1958, Sept.–Oct., v. 9, No. 5, 191–6, 3 figs.

Deoxyribonuclease (DNase) activity was determined by spot inoculation of culture plates containing 2 mgm. per ml. DNA and 0·8 mgm. per ml. calcium chloride, and flooding of the incubated plates with N hydrochloric acid. A clear zone in the otherwise opaque plate indicated DNase activity. 200 coagulase-positive staphylococci and 104 coagulase-negative strains were tested; all the coagulase-positive strains, but none of the coagulase-negative strains, produced DNase. *R. E. O. Williams*

CASMAN, E. P. **Serologic Studies of Staphylococcal Enterotoxin.** *Pub. Health Rep.* Wash. 1958, July, v. 73, No. 7, 599–609, 5 figs. [31 refs.]

Staphylococci were grown with continuous shaking or aeration, in a medium based on Casamino acids, and sodium acetate, with added ferric citrate. Concentration and purification of enterotoxin from the culture filtrate were achieved by dialysis and pervaporation followed by methanol precipitation. Rabbits were immunized with these preparations; the antisera were able to confer passive protection on cats given an emetic dose of toxin, freed from haemolysins, intravenously.

Attempts were made to identify the antigen-antibody reaction in gel-diffusion plates. For this purpose the sera had to be absorbed to remove complicating antibodies but it was finally possible to reveal one antigen common to 21 strains of enterotoxigenic staphylococci and to 2 non-enterotoxigenic strains out of 29 strains of staphylococci examined. *R. E. O. Williams*

RICHOU, R., KOURILSKY, R. & CHIROL, C. Sur les propriétés toxigènes des staphylocoques conservés en présence de pénicilline et de streptomycine. [**Toxigenicity of Staphylococci held in Contact with Penicillin and Streptomycin for Long Periods**] *Rev. d'Immunologie*. 1958, Apr.–June, v. 22, No. 3, 136–41.

Two strains of *Staphylococcus aureus* were held in contact with various strengths of penicillin and streptomycin for periods between 75 and 222 days; they were then subcultured and tested for toxin production The prolonged contact with antibiotics had no detectable effect. *R. E. O. Williams*

COHEN, S. G., DZURY, D. S., MICHELINI, F. J., with the technical assistance of V. A. J. DRAPIEWSKI. **Immune Responses to** *Staphylococcus aureus* **Antigens.** *J. Infect. Dis.* 1958, July–Aug., v. 103, No. 1, 61–6, 2 figs. [18 refs.]

Rabbits were immunized with killed whole cells, cell protoplasm derived by ultra-sonic vibration, or pepsin-digested culture filtrate of the *Staphylococcus aureus* strain Wood 46. All the sera obtained were able to agglutinate whole cells, though to different titres. Attempts were made to study the antibodies in gel-diffusion plates. Antitoxin contained antibody to some protoplasmic antigen, and conversely. *R. E. O. Williams*

DÓBIAS, G. & BALLÓ, T. I. Der Staphylokokken-*alpha*-Antitoxintiter nicht pyodermischer Säuglinge, Kinder und Erwachsener. [**The Staphylococcal α-Antitoxin Titres in Infants, Children and Adults not suffering from Skin Infection**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, Oct., v. 116, No. 4, 372–83, 1 fig. [39 refs.]

Staphylococcus antitoxin titres were estimated on the sera of 500 persons of various ages, none of whom was suffering from a skin infection. The mean titre in newborn infants was 1·1 units per ml.; it fell to about 0·03 in infants of 1–3 months, and thereafter rose to about

1·1 in the 4–14-year group; adults had a slightly lower titre. At no age had more than about 6% a titre of over 2·5 units per ml. *R. E. O. Williams*

DRESSLER, J. A. W. **Value and Reliability of the Bacitracin Screen Test for identifying Lancefield Group-A Haemolytic Streptococci.** *South African Med. J.* 1958, Sept. 20, v. 32, No. 38, 945–6.

520 strains of haemolytic streptococci were tested for sensitivity to bacitracin and for reaction with Lancefield group A serum. Only 8 (2·1%) of the 383 bacitracin-sensitive strains were not group A, and only 5 (3·5%) of 137 bacitracin-resistant strains were group A.
R. E. O. Williams

HALPEREN, S., DONALDSON, P. & SULKIN, S. E. **Identification of Streptococci in Bacterial Mixtures and Clinical Specimens with Fluorescent Antibody.** *J. Bacteriology.* 1958, Aug., v. 76, No. 2, 223–4, 1 fig.

2 streptococcal group A antisera were coupled with fluorescein and used to stain streptococci from cultures and also to identify streptococci in direct smears from the throat. With cultures there was satisfactory specificity, apparently even without absorption of the serum. The smears from 33 patients infected with group A or C streptococci [proportion not stated] showed fluorescent-staining streptococci in 30 cases.
R. E. O. Williams

STOLLERMAN, G. H., KANTOR, F. S. & GORDON, B. D. **Accessory Plasma Factors involved in the Bactericidal Test for Type-Specific Antibody to Group A Streptococci. I. Atypical Behavior of Some Human and Rabbit Bloods.** *J. Exper. Med.* 1958, Oct. 1, v. 108, No. 4, 475–91, 2 figs. [15 refs.]

The bactericidal test for the detection of type-specific antibodies to group A streptococci depends upon the phagocytosis of the organisms when grown in fresh human blood containing homologous M antibody [this *Bulletin*, 1958, v. 33, 173]. Rabbit and mouse blood are only weakly bactericidal under conditions of this test. When testing rabbit serum for the presence of specific antibodies it is necessary to carry out the indirect test [*ibid.*, 1957, v. 32, 201], the rabbit serum being added to normal human blood before addition of the organisms.

Blood from 2 out of 25 healthy persons consistently failed to produce a strong bactericidal test. The defect was associated with the plasma since blood cells from these individuals behaved normally when suspended in suitable plasma and leucocytes suspended in these atypical plasmas showed delay in phagocytosis in the first 1–2 hours.

2 rabbits were found whose blood was strongly bactericidal against streptococci in the presence of type-specific antibody of rabbit or human origin. The authors suggest that the atypical behaviour of some human and rabbit bloods may be due to variations in accessory plasma factors, influencing the rate of phagocytosis of streptococci in this test.
M. Patricia Jevons

PAKUŁA, R., FLUDER, Z., HULANICKA, E. & WALCZAK, W. **Studies on Transformation of Streptococci.** *Bull. Acad. Polonaise des Sci.* Warsaw. Ser. Sci. Biol. 1958, v. 6, No. 8, 319–23.

Bacterial DNA was prepared from various strains of streptococci that had been trained to streptomycin resistance, by extraction with the lytic enzyme mixture obtained from *Streptomyces albus*; the nuclease was inhibited with sodium citrate. Attempts were then made to convert various streptococci to streptomycin resistance by treatment with the DNA. 13 of 45 strains of *viridans* streptococci were transformed as was 1 group H streptococcus, but none of 16 *Str. salivarius* nor various haemolytic streptococci. *Viridans* streptococci, *Str. salivarius*, *Str. s. b. e.*, haemolytic streptococci and an enterococcus all proved efficient as donors. [There are no details on the frequency with which transformed clones were found.] *R. E. O. Williams*

PAKUŁA, R., HULANICKA, E. & WALCZAK, W. **Transformation Reactions between Streptococci, Pneumococci, and Staphylococci.** *Bull. Acad. Polonaise des Sci.* Warsaw. Ser. Sci. Biol. 1958, v. 6, No. 8, 325–8.

With the methods described by PAKUŁA *et al.* [see above] attempts were made to use pneumococci and staphylococci in transformation reactions. Streptomycin resistance could be transferred from the pneumococcus to various streptococci, but from the staphylococcus only to a *Str. s. b. e.* and a group H streptococcus. *R. E. O. Williams*

KÖHLER, W. & MOCHMANN, H. Streptokokkenbefunde der Tonsillen und Antistreptolysintiter bei Schlachtschweinen. [**Isolation of Streptococci from the Tonsillar Region, and Antistreptolysin Titres in Pigs**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 58–68. [25 refs.]

139 strains of streptococci were isolated from the tonsillar region of 100 pigs. 37 belonged to group D and 12 were ungroupable but physiologically similar. 31 strains were group B. No strains of group A were found though a number of strains giving a positive CAMP test gave apparently non-specific cross-reactions with group A sera. Small numbers of strains of groups C, G, F, K, N and P were found, as well as a number of ungroupable streptococci.

The antistreptolysin titre was in all cases less than 22 units per ml. *R. E. O. Williams*

RICHOU, R. & RICHOU, H. Sur le titrage de l'antistreptolysine des sérums. [**Titration of Antistreptolysin in Serum**] *Rev. d'Immunologie.* 1958, Apr.–June, v. 22, No. 3, 146–50.

The authors describe their technique for antistreptolysin determinations, which does not differ greatly from other widely used methods. The streptolysin is tested against a standard serum. The test serum is diluted [in an irregular series], incubated with the streptolysin for 1 hr. at 37°C. before the addition of the red cells and further incubation for 3/4 hours. The last tube

showing any trace of haemolysis is taken as the end point. *R. E. O. Williams*

MERGENHAGEN, S. E., THONARD, J. C. & SCHERP, H. W. **Studies on Synergistic Infections. I. Experimental Infections with Anaerobic Streptococci.** *J. Infect. Dis.* 1958, July–Aug., v. 103, No 1, 33–44, 6 figs. [28 refs.]

6 strains of strictly anaerobic streptococci were tested for their ability to produce lesions when injected intracutaneously into rabbits. 1, which formed hyaluronidase, gave an erythematous spreading lesion with central abscess; the others gave no more than localized lesions. The minimal infecting dose of the organisms suspended in saline was about 10^8; when suspended in saline containing 0·1% thioglycollate and 0·1% agar, 2 of the strains could give lesions from a dose of 10^5. Much more extensive lesions were produced when the streptococci were mixed with a suspension of staphylococci before injection. The streptococcus or the staphylococcus alone produced a localized abscess; together they produced a lesion with a necrotic centre and an advancing erythematous edge. Enhancement of the streptococcol lesions could also be produced by staphylococcal culture filtrates and this was thought to be due partly to the contained hyaluronidase, and partly to some other unidentified heat-labile factor. Testicular hyaluronidase enhanced the lesion, though in a different way; streptococcal hyaluronidase had no effect. *R. E. O. Williams*

WUNDT, W. Die Typenbestimmung von Brucellen und ihre Bedeutung für die Systematik des Genus *Brucella*. [**Typing of Brucellae and its Importance in the Systematics of the Genus Brucella**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 3, 235–51, 4 figs. [Numerous refs.]

An extensive review of the methods recommended in *Brucella* typing is presented. Sugar fermentation and CO_2 dependence are discarded as unreliable tests. Dye sensitivity, H_2S production, splitting of urea, the "sodium diethyl dicarbamate test" of Renoux (DEDTC test), and typing with monospecific sera are retained and the methods of employing these are described in detail.

An extensive table is presented showing the correlation of these tests for 164 strains including 16 isolated by blood culture in human infections and the remainder sent for typing or obtained from collections maintained in laboratories in both hemispheres. Among these 50 could be frankly classified as *Br. melitensis* type I, 33 as *Br. abortus* type I, 18 as *Br. suis* type I (originally described as American type) and 18 as *Br. suis* type II (originally described as Danish type). The remainder showed divergence from the classical types being, *e.g.*, *melitensis* in respect of dye sensitivity, absence of H_2S and the DEDTC test but *abortus* in respect of absence of urease and by monospecific serum agglutination.

The general conclusion drawn is that the types represent varieties rather than species.

There are 3 good photographs illustrating typical differentiations by the DEDTC test. *J. W. McLeod*

ABERNATHY, R. S., BRADLEY, G. Mary & SPINK W. W. **Increased Susceptibility of Mice with Brucellosis to Bacterial Endotoxins.** *J. Immunology.* 1958, Oct., v. 81, No. 4, 271–5. [19 refs.]

The observation that human subjects previously infected with brucellae were more susceptible to the toxic action of brucella endotoxins than control uninfected subjects [this *Bulletin*, 1958, v. 33, 657] prompted the authors to study the effect of administered endotoxins in mice previously infected with brucellae. Infected mice challenged with endotoxin 2 weeks after infection did not survive a dose which was not lethal for uninfected mice. With a fixed dose, a peak sensitivity is found at 2–4 weeks after infection, time to death being also shorter. Mice appeared ill 2 hours after receiving the endotoxins and all deaths occurred within 48 hours. There was no correlation between susceptibility to brucella endotoxin and extent of infection as indicated by quantitative spleen cultures. Sensitivity also developed for typhoid and coli endotoxins, this heterologous susceptibility persisting for 8 weeks.

The surmise that administration of endotoxin directly enhances infection, converting a dormant into a lethal one [*ibid.*, 1958, v. 33, 270] does not appear acceptable, a satisfactory explanation of the phenomenon being still wanting. *E. Agius*

SPINK, W. W. & ANDERSON, Dorothy. **Infection of Mice with G Variants (Micro-Colonies) of** *Brucella abortus*. *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 466–70.

"The foregoing data show that pure cultures of micro-colonies can be isolated readily from smooth strains of *Br. abortus*. These G cultures can be maintained for several generations if subcultures are incubated aerobically. When fresh transplants are incubated in an atmosphere of 10% CO_2 reversion to the large colonial form occurs. Mice can also be easily infected with G colonies and the small forms can be recovered from the tissues, though the infection is of low pathogenicity and of relatively brief duration. The practical significance of these observations in animal and in human brucellosis under natural conditions cannot be ascertained at this time. Huddleson and Baltzer (*Studies in Brucellosis* III, 1952. Mich. State College Agr. Exp. Station, Lansing) did report the presence of G colonies of *Br. abortus* in a culture of stomach contents of an aborted bovine fetus, and Hall and Spink [this *Bulletin*, 1947, v. 22, 591] isolated *Br. abortus* G colonies from a human patient. On several occasions we observed the presence of small colonies in cultures of *Br. melitensis* isolated from tissues of mice. It is suggested that a more intensive study should be made of fluids and tissues of animals and man for presence of small colonial forms of brucellae."

SPINK, W. W. & ANDERSON, Dorothy. **Influence of Cortisone on Infection in Mice caused by Strain 19** *Brucella abortus*. *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 470–71.

"An acute infection with strain 19, *Br. abortus* was established in mice. Simultaneous treatment with

cortisone enhanced the infection, but did not interfere with the formation of brucella agglutinins. However, cortisone did not cause the severe necrosis of the hepatic parenchyma and proliferation of brucellae that had been previously observed in studies with a more virulent species of Brucella."

PANNELL, Lolita. **Studies on Protection against Experimental Tularemia in Mice. I. Altered Susceptibility of White Mice to Tularemia following** *Hemophilus pertussis* **Vaccination.** *J. Infect. Dis.* 1958, Mar.–Apr., v. 102, No. 2, 162–6. [16 refs.] **II. Immunogenicity of** *Bacterium tularense* **Filtrates in Mice and Enhancement by** *Hemophilus pertussis* **Vaccine.** *Ibid.*, 167–73. [16 refs.]

I. An alteration was observed in susceptibility and resistance of white mice to tularaemia after vaccination with *Haemophilus pertussis*. Inoculation of pertussis vaccine before infection increased the resistance of mice to a challenge dose of approximately 100 LD50 of a moderately virulent strain of *Brucella tularensis*. Simultaneous inoculation of pertussis vaccine and the challenge dose increase the susceptibility of the mice to infection with the *Br. tularensis*. The combination of pertussis and tularensis vaccines, however, gave better protection against a low challenge dose of tularaemia than that given by tularensis vaccine alone. The value of pertussis vaccine as an adjuvant has been discussed.

II. Crude filtrates from broth cultures of *Br. tularensis* gave protection against experimental tularaemia in mice when a strain of moderately low virulence was used for challenge. All strains of *Br. tularensis* produced the protective substance which was as effective as *Br. tularensis* vaccine. The protection given by the filtrates was increased by the simultaneous inoculation of *Haemophilous pertussis* vaccine. *F. T. Perkins*

CAMERON, H. S. & MEYER, Margaret E. **Metabolic Studies on** *Brucella neotamae* (Stoenner and Lackman). *J. Bacteriology*. 1958, Nov, v. 76, No. 5, 546–8.

"The species *Brucella neotamae* was isolated from the wood rat and identified as a new species by Stoenner and Lackman on the basis of conventional methods for speciating the genus *Brucella*. These observations were substantiated by manometric techniques in that the oxidative metabolic pattern of the proposed new species is not identical to the patterns of any of the three recognized species."

TE PUNGA, W. A. & PRESTON, N. W. **Intratracheal Infection of Mice with** *Haemophilus pertussis*. *J. Path. & Bact.* 1958, July, v. 76, No. 1, 275–83, 1 fig. on pl. [13 refs.]

A new technique for the intratracheal inoculation of mice with *Haemophilus pertussis* has shown a high degree of consistency in its ability to establish lethal pulmonary infections. Intratracheal inoculation is given with a modified Pasteur pipette introduced through the mouths of mice anaesthetized with nembutal. The relative merits of this technique and that of intranasal instillation are discussed. Active and passive immunity to pulmonary infections effected by the intratracheal route has been demonstrated. *F. T. Perkins*

SEKI, T., MAEJIMA, K., MAKI, S., KITADA, A. & MAEDA, K. **Studies on Whooping Cough by the Intratracheal Inoculation Method.** *Med. J. Osaka Univ.* 1958, Feb., v. 8, Nos 2/3, 257–77, 29 figs. on 5 pls. & 1 chart. [29 refs.]

The intratracheal method of inoculation of *Haemophilus pertussis* into mice already described by the authors [this *Bulletin*, 1954, v. 29, 1261] has been used to follow the histological changes in the lungs associated with bacterial proliferation. One week after an inoculum of 5,000 organisms the bacterial count had increased to about 10^8 and bacteria were found in the alveoli; cellular infiltration of polymorphonuclear leucocytes had also occurred. After the fourth week active phagocytosis could be seen and the bacterial count decreased. Interstitial inflammation was still present in the tenth week and at this time the signs of bronchopneumonia and intrapulmonary bacteria had disappeared. The haemorrhagic pneumonia and death of mice occurring as a result of a large dose of organisms can be attributed to pertussis toxin.

F. T. Perkins

URANO, N. **Study on the Hemolytic Phenomenon of** *Hemophilus pertussis*. *Japanese J. Microbiol.* 1958, Jan., v. 2, No. 1, 101–6, 3 figs. & 1 diagram.

The substance responsible for the haemolysis observed on a Bordet-Gengou plate after the growth of *Haemophilus pertussis* has been shown to be a heat-stable, non-toxic metabolite. The author has named this substance pertussallysin, which has been distinguished from the heat-labile toxin. *F. T. Perkins*

MOTA, I. **Mast Cell and Histamine in Rat Anaphylaxis: the Effect of** *Haemophilus pertussis*. [Correspondence.] *Nature*. 1958, Oct. 11, v. 182, 1021–2. [10 refs.]

Inoculation with *Haemophilus pertussis* vaccine renders mice and rats hypersensitive to anaphylaxis as well as decreasing their resistance to histamine and serotonin. Since most of the tissue histamine is located in the mast cells which, in these animals, are rich in serotonin, and since anaphylaxis in the rat produces mast cell damage and release of histamine, the author studied the behaviour of these cells in anaphylaxis of rats treated with *H. pertussis*.

2 groups of rats were studied, one in which horse serum alone was injected and the other in which *H. pertussis* vaccine was given in addition to horse serum. Both groups were challenged with horse serum and blood samples taken 5 minutes later for histamine estimations on the guineapig ileum. The rats were killed and frozen sections prepared from the skin of the snout, lips and tongue, and mast cell damage was estimated by the percentage of cells showing granule

extrusion. It was shown that *H. pertussis* enhances the sensitivity to anaphylaxis so that mast cell disruption and appearance of histamine in plasma resulted after injection of antigen. The mechanisms responsible for these phenomena are discussed. *F. T. Perkins*

UCHIDA, T., YAMAGUCHI, Y., NAGAI, M., KIKUCHI, T., HAYASHI, Y., KOGANEZAWA, S. & TSURUGAYA, M. **Effects of *Haemophilus pertussis* and its Cell Components upon the Blood Picture of the Rabbit.** *Gunma J. Med. Sci.* Maebashi. 1958, June, v. 7, No 2, 127–33, 8 figs. [16 refs.]

The effect on the blood picture of an intravenous injection of *Haemophilus pertussis* cells and *pertussis* extracts has been studied.

An increase in the count of leucocytes and lymphocytes occurred with phase I cells as well as with *pertussis* toxin. A similar, though more transient, rise in counts occurred with both phase III cells and heated toxin. The rise in the number of lymphocytes caused by phase I cells was prevented by injection of an antitoxic serum and the author therefore attributes this rise to *pertussis* toxin. Agglutinogen, polysaccharide and lipid extracted from the bacteria had no effect upon the blood picture. *F. T. Perkins*

MAITLAND, H. B. & GUÉRAULT, A. **Some Surface Components of *Haemophilus pertussis*: Immunising Antigen, Histamine-Sensitising Factor and Agglutinogen.** *J. Path. & Bact.* 1958, July, v. 76, No. 1, 257–74, 1 fig. [15 refs.]

Saline washings of *Haemophilus pertussis* organisms were shown to protect mice against intracerebral challenge and to contain histamine-sensitizing factor (HSF) as well as agglutinogen. The bacteria washed with saline, however, retained all these properties. Treatment of the bacteria with a mixture of thiourea, urea and formamide removed more material than washing with saline since the bacteria then lost their HSF, although they still protected mice and contained agglutinogen. The authors have investigated the extracts and treated bacteria for their ability to protect mice, to sensitize to histamine and to agglutinate after treatment by filtration, freeze-drying and dialysis, and they have studied their ultraviolet absorption spectrum and chemical analysis. *F. T. Perkins*

COHEN, H. H. **Establishment of a Dried Standard *pertussis* Vaccine.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1958, v. 24, No. 1, 33–48. [16 refs.]

The intracerebral mouse-protection test was used to compare the potency of a Dutch standard pertussis vaccine B with the United States standard No. 4. The values obtained were confirmed by assays in Holland and the U.S.A., and a value of 3·7 units/ml. was given to the standard.

The reasons are discussed for giving a unit value to a standard, although this unit value cannot be determined accurately in a biological test. *F. T. Perkins*

LOGAN, J. E., GRIFFITHS, B. W. & MASON, M. A. **Studies on the Clearance of Radioiodinated *pertussis* Vaccine from the Lungs of Immunized and Non-Immunized Mice following Intratracheal Administration.** *Canadian J. Microbiol.* Ottawa. 1958, Aug., v. 4, No. 4, 321–7. [12 refs.]

The use of radio-iodinated pertussis vaccine has shown that an intratracheal route of administration gives a more reproducible inoculum into the lungs of mice than that given by intranasal administration.

Mice immunized intraperitoneally with a single dose of pertussis vaccine and then given radio-iodinated vaccine by intratracheal administration cleared a significantly higher amount of radio-activity from their lungs than non-immune mice. This effect occurred as early as 1 day after immunization. It was also found that mice immunized 6 to 30 days before an intratracheal challenge of labelled vaccine showed higher fresh weights of their lungs than non-immune mice. The significance of these results is discussed.

F. T. Perkins

OSIPOVA, P. V. **The Causative Organism of Bronchisepticosis and its relation to *Haemophilus pertussis*. Cultural and Antigenic Characteristics of *Brucella bronchiseptica*.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 9/10, 1508–13. [11 refs.] [Translated from Russian.]

The author found that *Brucella bronchiseptica* could be isolated from the respiratory tract of a high proportion of animals of different species after experimental infection with *Haemophilus pertussis*. In common with previous workers [see, for example, this *Bulletin*, 1953, v. 28, 664; 1954, v. 29, 668 *bis*], he found that the antigenic structure of the *Br. bronchiseptica* strains isolated from these animals was closely related to that of *H. pertussis*. All freshly isolated strains of *Br. bronchiseptica* were in phase I but on storage passed into phase IV. Organisms in these 2 phases showed different cultural and antigenic features and a different degree of antigenic relationship to *H. pertussis*.

F. T. Perkins

LESHKOVICH, L. I. **The Action of X-Rays on the Virulence and Antigenic Properties of *Pasteurella pestis*.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 1/2, 199–204. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 438.]

JANSSEN, W. A., FUKUI, G. M. & SURGALLA, M. J. **A Study of the Fate of *Pasteurella pestis* following Intracardial Injection into Guinea Pigs.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 183–7, 2 figs. [22 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 437.]

SELENKA, F. Über die Abgrenzung von *Ps. aeruginosa* gegen *Ps. fluorescens* und *Ps. putida* auf TTC-Nährböden. [**The Differentiation of** *Pseudomonas pyocyanea* **from** *P. fluorescens* **and** *P. putida* **on TTC Medium**] *Arch. f. Hyg. u. Bakt.* 1958, Dec., v. 142, No. 8, 569–74, 1 fig. [10 refs.]

The English summary appended to the paper is as follows:—

"Ps. aeruginosa exhibits a resistance of high degree against TTC. This property has been used for the differentiation of Ps. aeruginosa from Ps. fluorescens and Ps. putida. On an agar medium containing TTC in concentrations of 1:100 and 1:500, as described in this paper, 265 strains of Ps. fluorescens, 33 strains of Ps. putida and 35 strains of Ps. aeruginosa have been clearly differentiated following incubation at 37° and 42°."

WOLFF, J. W. & BOHLANDER, H. J. **Serological Classification of Pathogenic Leptospires. Analysis and Comparison of Six Strains related to Serotypes of the** *hebdomadis* **Serogroup.** *Trop. & Geograph. Med.* Amsterdam. 1958, Mar., v. 10, No. 1, 37–46. [22 refs.]

A detailed study was made of the serological characteristics of 6 strains of leptospires which other workers had reported as having affinities with one or more of the serotypes belonging to the Hebdomadis serogroup. The names of the strains were as follows:—Kremastos and Szwajizak [SMITH *et al.*, this *Bulletin*, 1955, v. 30, 763], Barthélémy, Jules and Kabura [VAN RIEL *et al.*, *ibid.*, 1956, v. 31. 909] and Sari [BABUDIERI, *ibid.*, 1957, v. 32, 502]. Babudieri [*loc cit.*] concluded that strains Sari and Szwajizak represented, respectively, the "complete and incomplete biotypes" of a new serotype which he named *Leptospira mini*.

The present authors give protocols of the extensive series of agglutination-lysis and cross-agglutination tests made with these strains [the original should be consulted by those interested in the antigenic composition of leptospires]. Their results confirmed Babudieri's findings with strains Sari and Szwajizak, and they found that strain Barthélémy was the "complete biotype" of *L. mini*. They considered that the remaining 3 strains represented new serotypes which they propose to name *L. jules* (type strain Jules), *L. kabura* (type strain Kabura) and *L. kremastos* (type strain Kremastos).

J. C. Broom

VARFOLOMEEVA, A. A. **The Properties and Nomenclature of** *L. perepelitsin*, **a Causative Agent of Benign Leptospirosis.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 1, 50–56, 1 fig. [12 refs]

The antigenic characteristics of strains of a leptospiral serotype known variously in the U.S.S.R. as *Leptospira perepelitsin*, *L. tarassovi*, *L. DV-A*, strain T384 and strain PK-20 were compared with those of strains of *L. hyos* isolated respectively in Argentina, Australia and Finland. From the results of agglutination and cross-immunity tests the author concludes that the U.S.S.R. strains are identical with *L. hyos*, thus confirming the work of KMETY (*Zent. f. Bakt.* I. Abt. Orig. 1955, v. 163, 464).

The first strain of this serotype was isolated in 1938 and was investigated from 1939–41 by various workers who decided that it differed antigenically from the other serotypes then known in the U.S.S.R. The epithet *perepelitsin* was proposed by TERSKIKH in 1945 [so far as the reviewer can make out from text and references]. The author suggests that the serotype should be named *L. tarassovi* [*sic*] in honour of TARASOV [*sic*] who first discovered it.

[The author's proposal is not in accordance with the International Code of Nomenclature of Bacteria and Viruses (1958). The epithet *hyos* was proposed for this serotype by SAVINO and RENNELLA in 1944 (*Día médico*, v. 16, No. 43, 1295). Principle 9 of the Code states that "In species the correct name is the binary . . . combination of the generic name with the earliest available epithet validly published with the same rank." If *perepelitsin* was first *published* in 1945, *hyos* undoubtedly has priority since the date of *isolation* is of no importance. Whatever be the final decision about the relative claims to priority of *hyos* and *perepelitsin*, there is certainly no justification for the proposal to rename the serotype *L. tarassovi*.] *J. C. Broom*

KAUFMAN, L. & HUMPHRIES, J. C. **Studies of the Nutritional Requirements of** *Clostridium tetani*. **I. A Chemically Defined Medium.** *Applied Microbiol.* Baltimore. 1958, Sept., v. 6, No. 5, 311–15. [15 refs.]

Four strains of *Clostridium tetani* were employed to ascertain the essential growth requirements of the organism. A semi-synthetic medium containing 39 constituents was developed which was capable of supporting good growth, but when all vitamins or all nitrogen bases or the casamino acids were omitted no growth was obtained. The essential requirements were then ascertained by omission of one or other of constituents and it was found that biotin, pyridoxamine, nicotinic acid, calcium pantothenate, folic acid and uracil were essential for growth whereas riboflavine, vitamin B12, para-aminobenzoic acid, sodium oleate and the purines xanthine and guanine were non-essential. The need for thiamine, inositol and adenine varied from strain to strain. Inconsistent growth was obtained when the casamino acids were replaced with pure amino acids. This was not due to oxidation-reduction effects. *P. A. Clearkin*

GUHA, S. R., CHAKRAVARTI, H. S. & GHOSH, J. J. **Studies on Brain Metabolism: Action of Tetanus Toxin on the Acetylcholine System of Rat Brain.** *Ann. Biochem. & Exper. Med.* Calcutta. 1958, v. 18, No. 4, 113–16. [15 refs.]

"1. Dialysed tetanus toxin produces a large decrease in the rate of synthesis of bound acetylcholine by slices of rat-brain cortex in presence of glucose. The synthesis of acetylcholine is also decreased.

"2. The administration of dialysed tetanus toxin, to produce convulsion in rats, caused a significant decrease in the acetylcholine level of the brain."

MEISEL, H., TREMBOWLER, Paulina & POGORZELSKA, Barbara. Aglutyniny i przeciwciałna niekompletne dla *Clostridium perfringens* typu a w surowicach ludzkich. [**Agglutinins and Incomplete** *Clostridium perfringens* **Type A Antibodies in Human Serum**] *Med. Dośw. i Mikrob.* Warsaw. 1958, v. 10, No. 4, 431–9. [12 refs.]

The English summary appended to the paper is as follows:—

"202 sera of healthy and diseased adults were examined as to the presence of antibodies agglutinating *Cl. perfringens* type A strains. The well known strain SR_{12} was as the only agglutinated. A percentage of sera as high as 70% appeared to be able to agglutinate the bacilli to a higher or lesser degree. The sensitized SR_{12} cells were then used in the antiglobulin (Coombs) test. 93% of sera were proved to contain the so called incomplete antibodies. By a more detailed analysis it could be shown that 6 out of the examined sera did not contain either the agglutinins or the incomplete antibodies; 62 sera appeared to contain the incomplete antibodies only without agglutinins; a deficiency of incomplete antibodies and the presence of agglutinins was shown in 7 sera; the presence of both kinds of antibodies was observed in 127 sera. The antiglobulin test carried out with sensitized cells of *Cl. perfringens* type A strains, never agglutinated by the examined sera (f.e. BP_6K, SS) appeared to yield positive results too. Incomplete antibodies were never inactivated when heated 60 min. at 56°C or 20 min. at 60°C. The antibodies were scattered equally regardless of sex. No connection between the appearance of antibodies and kind of sickness could be observed."

MOUSSA, R. S. **Complexity of Toxins from** *Clostridium septicum* **and** *Clostridium chauvoei*. *J. Bacteriology*. 1958, Nov., v. 76, No. 5, 538–45. [34 refs.]

"*Clostridium septicum* and *Clostridium chauvoei* produce more than one toxic substance. The number and type of these components vary, among other things, with the strain of the organism, the culture medium used, and the length of the incubation period.

"The lethal, necrotic, oxygen-stable hemolysin (α-toxin) of *C. septicum* is specific for this organism; it is neutralized by homologous antisera, but not by antisera of *C. chauvoei* or by normal sera. Smaller amounts of substances possessing oxygen-stable hemolytic as well as necrotizing activity were similarly detected in filtrates of *C. chauvoei*.

"The deoxyribonucleases of *C. septicum* and *C. chauvoei* (β-toxin) were found distinct from the α-toxins, and from the hyaluronidases (γ-toxins) of these organisms. At least 2 deoxyribonucleases and 2 hyaluronidases are shared by their filtrates.

"The oxygen-labile hemolysins (δ-toxins) are similarly related but are not identical. They are readily produced by most strains and are reversibly inactivated by oxidation and reactivated by reduction. They are neutralized by anti-streptolysin-O as well as by normal sera. Mouse erythrocytes were relatively more resistant than rabbit erythrocytes to the hemolytic action of the oxygen-labile hemolysin."

TREADWELL, P. E., JANN, G. J. & SALLE, A. J. **Studies on Factors affecting the Rapid Germination of Spores of** *Clostridium botulinum*. *J. Bacteriology*. 1958, Nov., v. 76, No. 5, 549–56, 7 figs. [20 refs.]

"The germination of spores of *Clostridium botulinum* has been studied using changes in heat lability, refractive index, and staining properties as criteria for germination. Complete germination has been obtained within 2 hr in 5 per cent yeast extract, with outgrowth and multiplication in 4 hr. Complete germination has also been obtained in vitamin-free casamino acids. The necessity of sodium bicarbonate and the effect of heat activation on germination of this organism has again been demonstrated. A number of enzyme inhibitors and antibiotics have been shown not to be effective in the initial steps of germination. The implications of these results have been discussed. It is suggested that the first step in germination is a change in the permeability of the spore coat, possibly mediated by a heat activated proteinase. Leakage of spore material then causes the change in refractive index and heat lability."

BOYLES, W. A. & LINCOLN, R. E. **Separation and Concentration of Bacterial Spores and Vegetative Cells by Foam Flotation.** *Applied Microbiol.* Baltimore. 1958, Sept., v. 6, No. 5, 327–34, 3 figs. [18 refs.]

Selective methods for removing or concentrating bacterial spores and vegetative cells from the growth medium were developed after observation of the fact that masses of "clean" spores collected in the head of foam when *Bacillus anthracis* was grown in aerated deep cultures.

Foam was produced by passing compressed air through fritted glass into the culture. Cultures were incubated in Erlenmeyer flasks on a reciprocating shaker and sterile compressed air was passed through them into the foam chambers. Studies were made on the effect of size of pores of spargers, rate of air flow and other variables on the collection of spores.

The selective nature of foam flotation appears to furnish much cleaner spores than does centrifugation. To obtain clean batches of spores foam flotation, centrifugation and precipitation by gels should be combined. *P. A. Clearkin*

LEONARD, C. G., HOUSEWRIGHT, R. D. & THORNE, C. B. **Effects of some Metallic Ions on Glutamyl Polypeptide Synthesis by** *Bacillus subtilis*. *J. Bacteriology*. 1958, Nov., v. 76, No. 5, 499–503. [12 refs.]

FUNGI

LARSH, H. W. & SHEPARD, C. C. **HeLa Cells and** *Histoplasma capsulatum*. **Phagocytosis and Subsequent Intracellular Growth.** *J. Bacteriology*. 1958, Nov., v. 76, No. 5, 557–63, 6 figs. [12 refs.]

"Horse sera that had been selected for their ability to promote phagocytosis of tubercle bacilli by HeLa

cells, when incorporated into the tissue culture medium, did not enhance phagocytosis of the yeast phase of *Histoplasma capsulatum* by these cells.

"When sera of a number of species were studied as components of the tissue culture fluid, it was found that fresh guinea pig serum resulted in the greatest phagocytosis of the fungus. The sera of calves, monkeys, and rabbits were ineffective, and those of chickens and dogs were intermediate. Some human sera had intermediate value and some produced little phagocytosis.

"In these preliminary experiments the sera of human patients with histoplasmosis did not seem noticeably more or less effective. There appeared to be no relationship to the antibody response of the patient, nor to the susceptibility of the species to the disease. Heating serum to 56 C reduced its ability to promote phagocytosis of *H. capsulatum*.

"When a tissue culture medium containing 20 per cent fresh guinea pig serum was used for the HeLa cell cultures, they were found to be sensitive to small inoculum of *H. capsulatum*. An inoculum of 3 to 20 yeast phase organisms produced growth in monolayers of HeLa cells with colonies or plaques of infected cells that were detectable with low-power microscopy within 6 days."

COZAD, G. C. **A Study of the Whole Yeast Cell Agglutination Test in Rabbits experimentally infected with** *Histoplasma capsulatum*. *J. Immunology*. 1958, Nov., v. 81, No. 5, 368–75, 2 figs. [16 refs.]

"It was found that whole yeast cells of *Histoplasma capsulatum* grown on brain heart infusion agar at 37°C could be used as the antigen in a tube agglutination test with sera from rabbits experimentally infected with *H. capsulatum*.

"Very low or negative agglutinin titers were obtained with sera from infected rabbits using the commonly used incubation temperatures of 25, 37 or 52°C. Overnight refrigeration of tubes (4°C) resulted in slightly increased titers. Greater agglutinin titers were demonstrable in tubes that had been centrifuged, and it was found that an incubation period was not necessary using this technique. The method of choice was, therefore, to centrifuge the tubes immediately after mixing antigen with serum.

"Yeast cells from 3 strains of the fungus were shown to be useful agglutinogens, exhibiting approximately equal combining power. An additional strain was found to agglutinate spontaneously in normal human and rabbit sera.

"The methods used for inactivation (heat, formalin, and phenol) were found to have an effect upon the agglutinating ability of cells from the different strains, but no one method seemed to be the best for all strains tested.

"In sera from rabbits experimentally infected with *H. capsulatum*, agglutinin titers were found to rise rapidly during the first week of the disease, reach a maximum by the end of the second week, and become negative at the end of a 9 week period. Complement fixation tests using whole cell antigens were also positive after 1 week, but reached a peak at 6 weeks and remained positive in high titers at the end of 13 weeks.

"The histoplasma agglutination antigen when tested in sera of rabbits experimentally infected with *Blastomyces dermatitidis*, *Sporotrichum schenckii*, *Candida albicans* and *Coccidioides immitis*, gave positive results only with *B. dermatitidis*.

"No differences in specificity of the antigens were noted after treatment with formalin and phenol or heat inactivation.

"A macroscopic slide agglutination test is described which proved of value in "screening" rabbit sera for the presence of antibodies against yeast cells of *H. capsulatum*."

RICKETTSIAE

REHN, F. **The Relationship between** *Coxiella burneti* **and some Ticks, with special reference to the Species** *Ixodes ricinus*. *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 3, 300–13, 1 fig. [62 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 431.]

KULAGIN, S. M., FEDOROVA, N. I. & SOKOLOVA, N. F. **The Survival of** *Rickettsia burneti* **in Water and Methods of Disinfection.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 1/2, 225–30. [12 refs.] [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 430.]

KIREEVA, R. A. **The Serological Diagnosis of North Asiatic Tick-Borne Typhus Fever.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 1/2, 235–8. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 428.]

BACTERIOPHAGES

LANDY, M., TRAPANI, R. J. & SHEAR, M. J. **Interference by Endotoxic Polysaccharides with Inactivation of Coliphage by Human Serum.** *Brit. J. Exper. Path.* 1958, Dec., v. 39, No. 6, 618–30, 5 figs. [19 refs.]

Properdin is usually assayed by its interaction with polysaccharides. The authors have shown that various polysaccharides from bacteria, plants or animals inhibited the neutralizing action of normal human serum against T2r+ phage. Inhibition was not caused by the

destruction of complement or any of the other substances required by the properdin system, but resulted apparently from reaction with properdin itself. The degree of inhibition of phage neutralization was a linear function of the dose of polysaccharide, within a range of 1–30 μgm. Thus the method can be used for comparing the potency of different polysaccharide preparations. Pooled human serum was used, as not all sera were satisfactory. It was also found that incubating serum at 37°C. for 1 hour increased its phage-neutralizing activity.

[See also this *Bulletin*, 1958, v. 33, 992 *bis*.]

Janice Taverne

CHASE, Martha & DOERMANN, A. H. **High Negative Interference over Short Segments of the Genetic Structure of Bacteriophage T4.** *Genetics.* 1958, May, v. 43, No. 3, 332–53, 4 figs. [28 refs.]

The results of biparental crosses between mutants of the *r* II region of T4B phage involving 2, 3 or 4 factors establish that the mutants in a given cistron or functional group are arranged in linear order. It is also shown that those phage recombinants which occurred more frequently than was predicted and which resulted from more than one gene exchange (a phenomenon called "high negative interference") followed multiple exchanges within short segments of the chromosome, and that the frequency of these events was greater the smaller the genetic region under study. The authors rule out the possibility that this phenomenon could be explained by gene reversion or conversion. [Compare EDGAR & STEINBERG, this *Bulletin*, 1959, v. 34, 173.] A detailed analysis of their results is given.

Janice Taverne

PARNAS, J., FELTYNOWSKI, A. & BULIKOWSKI, W. **Anti-*Brucella* Phage.** [Correspondence.] *Nature.* 1958, Dec. 6, v. 182, 1610–11, 2 figs.

This is a brief version of the paper reviewed in this *Bulletin*, 1958, v. 33, 1180.

NORTHROP, J. H., with the technical assistance of Marie KING. **Studies on the Origin of Bacterial Viruses. V. The Effect of Temperature on the Terramycin-Resistant and Phage-Producing Cells of *Bacillus megatherium* Cultures.** *J. General Physiol.* 1958, Nov. 20, v. 42, No. 2, 329–34, 3 figs.

"The growth rates, the mutation frequency rate constants of the terramycin-resistant cells, the burst size of the phage-producing cells, and the ratio of phage to cells all have a temperature coefficient of about 2 from 20 to 35° ($\mu = 9 \times 10^3$ calories), with a maximum at 40°.

"The mutation frequency rate constant (or time rate constant) of the phage-producing cells increases from 20 to 45° with a temperature coefficient of about 3 ($\mu = 2$ to 3×10^4 cal.).

"The change in the values for the growth rate, mutation rate, and cell volume occurs in less than 1 hour, after the temperature is changed. The value for the burst size of phage-producing cells changes for 3 to 4 hours.

"Prolonged growth of *megatherium* 899 at 48 to 50° results in the production of C + S phage, in place of T. Returning the culture to 25° results in the production of small T phage."

VIRUSES

In this section the abstracts are arranged as far as possible in the following order:—General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; Others.

HENLE, Gertrude; DEINHARDT, F.; BERGS, V. V.; HENLE, W. **Studies on Persistent Infections of Tissue Cultures. I. General Aspects of the System.** [HENLE, DEINHARDT, BERGS & HENLE]. *J. Exper. Med.* 1958, Oct. 1, v. 108, No. 4, 537–60, 3 figs. [36 refs.]

HeLa cells support the growth of many virus species and show obvious cytopathogenic changes. Other continuous culture lines of human cells such as MCN have a much more restricted range; only a few virus species will grow with recognizable cellular changes (vesicular stomatitis [VSV] actually yields 10–100 times higher titres in MCN than HeLa). Many viruses capable of infecting HeLa fail to grow at all in MCN, and others, *e.g.* Newcastle disease virus (NDV), grow but fail to produce any cytopathogenic effect.

MCN cells exposed to NDV become persistently infected; cell-line and virus can be propagated serially and simultaneously under the standard cultural conditions employed for the normal human cell-line. The nature of this type of virus-host cell relationship is the subject of this and the following 2 papers.

Provided the initial multiplicity of infection is less than 1, NDV causes no visible change in MCN. However, serial transfer of medium alone or medium plus cells over a period of 18 months still yielded virus detectable by assay on HeLa cells. In the persistently-infected cell-line MCN_{NDV} the total quantity of virus was low, considerably less than 1 particle per cell, and the medium alone accounted for only 1–10% of the total yield. There was no evidence of incomplete virus particle production.

The virus yield varied 100-fold over different samples of MCN_{NDV} suggesting fluctuations in cell-susceptibility, but attempts to enhance this process by changing the medium constitution or ultra-violet irradiation of the cultures were unsuccessful.

In comparison with the parent MCN, MCN_{NDV} cells showed a reduced growth-rate, increased aerobic glycolysis and diminished susceptibility to several cytopathogenic viruses—VSV, herpes simplex and influenza A. VSV titres were reduced by 10^7 times and even in infected tubes, virus growth did not continue to the 4+ degeneration seen in MCN cells.

Attempts were made to cure the persistent infection of MCN_{NDV} cultures by serial propagation in the

presence of specific immune serum. One culture-line was cured after 96 days' treatment, and did not relapse. However, in a second-line, although NDV gradually disappeared during 137 days' propagation in immune serum, the virus reappeared within 17 days of culture without antibody.

MCN populations were analysed by clone techniques to determine if they were heterogeneous with respect to NDV; 50 cloned lines showed exactly similar response to NDV challenge, *i.e.* persistent infection without cytopathogenic change, and acquired resistance to VSV. Similar cloning experiments with MCN_{NDV} populations yielded 39 lines; none contained NDV, all were susceptible to VSV and all responded to NDV challenge by developing persistent infection without cytopathogenic effect. Thus there was no evidence that persistent infection had led to selection of a particular cell-type from a heterogeneous parent culture.

The original NDV used for these experiments was an egg-adapted strain. On comparison with the virus strain recovered from established MCN_{NDV} cultures certain differences were observed—*e.g.* MCN-derived virus gave small fuzzy plaques on chick fibroblast monolayers unlike the large, clear plaques of the parent NDV. However, pathogenicity for the chick embryo or HeLa cells appeared to be unchanged.

[This long report is interspersed with fragmentary forays into other virus-host cell systems such as MCN_{6-6} MCN_{Mumps}, Lung-To_{NDV}, Lung-To_{6-6} and Lung-To_{Mumps}. All the results conform to the pattern described above, and the presentation of such a *tour de force* merely impedes the reader's grasp of the central problem.] *Derek Hobson*

BERGS, V. V., HENLE, Gertrude, DEINHARDT, F. & HENLE, W. **II. Nature of the Resistance to Vesicular Stomatitis Virus.** *J. Exper. Med.* 1958, Oct. 1, v. 108, No. 4, 561–72, 1 fig.

The preceding paper showed that MCN cells persistently infected with NDV become resistant to VSV, which grows to high titre in the parent MCN cell line with complete cellular disintegration. The present paper explores the possibility that this is a virus interference effect.

VSV was adsorbed equally well by MCN and by MCN_{NDV} cell suspensions, and apparently 97% of virus entering MCN_{NDV} cells underwent eclipse. Treatment of normal MCN cells with *Vibrio cholerae* receptor-destroying enzyme (to simulate one possible effect of the myxovirus NDV on the host cell) did not affect their susceptibility to VSV.

Comparative growth curve studies with VSV in MCN and MCN_{NDV} showed an increased eclipse phase and a 100-fold reduction of peak titre in the NDV-infected cell line. In the normal cell line, the rise to peak virus titre was accompanied by complete cell-sheet destruction; in MCN_{NDV} the cell sheet remained intact, and 3–4 days after the first phase of virus multiplication a second active phase occurred, again without cytopathogenic effect. However, when MCN_{NDV} cultures were reseeded (diluting 1 in 3) 14 days after exposure to VSV, complete cytopathogenic changes characteristic of VSV occurred within 2 days.

The fate of the carried virus NDV during VSV superinfection of MCN_{NDV} cells was observed by serial titration on HeLa cells or in chick embryos in the presence of high-titre antisera to VSV. The titre of NDV remained virtually constant despite the biphasic growth cycle of VSV and persisted until cell-destruction by VSV was well advanced.

It was found incidentally that VSV growth in MCN cells was highly susceptible to *p*H variations in the tissue culture medium; inoculation of tubes at an initial *p*H of 6·6 failed to produce cytopathogenic change within 3 days but once the medium *p*H was adjusted to 7·6 virus growth and cell-degeneration began promptly. These findings are relevant to the study of VSV growth in MCN_{NDV} cells since the persistently-infected cell line is known to show increased aerobic glycolysis. However, careful control of *p*H during VSV challenge of MCN_{NDV} cultures did not abolish their resistance to cytopathogenic infection; nor did the addition of lactic acid or sodium lactate to normal MCN cultures decrease their susceptibility to VSV.

Thus VSV is adsorbed by MCN_{NDV} cells and enters an eclipse phase; resistance is transitory and non-specific. These findings are in keeping with the hypothesis of viral interference. Further supporting evidence was obtained in experiments with NDV inactivated by ultraviolet irradiation. Normal MCN cultures treated with large concentrations of this product showed solid resistance to VSV challenge for a short period of time, but eventually VSV growth with cytopathogenic changes occurred. This gradual reversion to susceptibility was thought to be due to the accumulation of new non-resistant MCN cells, since cultures treated with inactivated NDV continued to multiply normally.

Derek Hobson

DEINHARDT, F., BERGS, V. V., HENLE, Gertrude, & HENLE, W. **III. Some Quantitative Aspects of Host Cell-virus Interactions.** *J. Exper. Med.* 1958. Oct. 1, v. 108, No. 4, 573–89, 4 figs. [11 refs.]

The data presented in the 2 preceding papers suggest that the majority of cells in the persistently infected MCN_{NDV} line behave differently from normal MCN cells. However, experiments described in this paper show that only occasional cells in MCN_{NDV} cultures actually contain infective particles as judged by the ability of whole cells or sonically-disintegrated cell material to transmit NDV infection to MCN or HeLa cells or to chick embryos. [This conclusion was confirmed by what appears to be an elegant modification of standard practice in the study of temperate bacteriophage systems.] Known numbers of MCN_{NDV} cells were plated on to monolayers of chick fibroblasts or HeLa cells, and agar overlays were then applied. Plaque counts after incubation showed that only 1 in 43 to 1 in 105 MCN_{NDV} cells was capable of yielding a plaque under these conditions. Comparison of plaque experiments with known numbers of intact MCN_{NDV} cells and with sonically-disintegrated cell suspensions indicated that active virus-producing cells seldom contained more than 1 infectious unit at any time.

The infrequency of cells containing multiple infectious units is also suggested from the patchy focal results

obtained by application of the haemadsorption technique of VOGEL and SHELAKOV [this *Bulletin*, 1957, v. 32, 1203] to MCN_{NDV} culture sheets.

NDV re-isolated after prolonged carriage in MCN_{NDV} cultures was known to differ from the parent egg-adapted NDV strain in its plaque morphology. Further study showed that the MCN-adapted NDV was of greater infectivity for normal MCN cells than the egg-adapted strain (producing noncytopathogenic persistent carriage) and therefore more capable of inducing resistance to VSV challenge.

In studies with MCN cultures freshly infected with NDV, the development of resistance to VSV was correlated with the NDV growth curve. Previous data suggested that 1 EID_{50} (50% infective dose for eggs) of NDV per cell is required for VSV resistance; however concentrations of NDV of that order were never obtained even from cultures showing solid resistance to VSV. The authors postulate that although there is no observable genetic heterogeneity in MCN cultures only a few cells in the culture are in the appropriate physiological state to permit virus reproduction. These "receptive" cells continue to produce and emit virus particles one at a time, and the process is extended as further cells enter the receptive phase or as new daughter cells are produced in the multiplying cell sheet. Virus titres do not rise to high levels because many infectious units are taken up by "refractory" cells. In these cells, NDV particles remain eclipsed and escape detection. However, these cells acquire resistance to VSV after NDV adsorption just as do "receptive" NDV-producing cells. A final speculation made by the authors is that persistently-infected cultures such as MCN_{NDV} may owe their resistance to unrelated viruses to products akin to interferon [ISAACS and LINDENMANN, this *Bulletin*, 1957, v. 32, 1203]. *Derek Hobson*

BADER, J. P. & MORGAN, H. R. **Latent Viral Infection of Cells in Tissue Culture. VI. Role of Amino Acids, Glutamine, and Glucose in Psittacosis Virus Propagation in L Cells.** *J. Exper. Med.* 1958, Nov. 1, v. 108, No 5, 617–30, 3 text figs. & 7 figs. on 2 pls. [16 refs.]

Mouse fibroblasts (L cells) depleted by cultivation for 2 days in a balanced saline medium, such as Earle's BSS, though susceptible to infection with psittacosis virus no longer supported its growth. This latent infection could be activated by the addition of the synthetic medium 635 of PARKER (*Canad. J. Biochem. and Physiol*, 1954, v. 32, 327). Virus appeared in the culture fluid on the 2nd day and by the 3rd day often exceeded the amount in the inoculum. The ingredients in Parker's medium essential to the multiplication of psittacosis virus were shown to be: tyrosine, threonine, methionine, isoleucine, phenylalanine, tryptophan, leucine, valine, cysteine, cystine and glucose. Lysine, arginine, histidine, hydroxproline, proline, glutamic acid, aspartic acid, serine, alanine and glycine were not essential even in combination. Neither glutamine nor glutamic acid was essential, but even in the presence of all the essential amino acids psittacosis virus would not multiply in the absence of glucose. Deprivation of the cell cultures for 2 days of phenylalanine or tryptophan rendered them incapable of supporting the growth of psittacosis virus. Though the cells on deficient media showed degenerative changes there was no strict correlation between the appearance of the cells and their suitability for virus multiplication.

[For earlier parts of this study, see this *Bulletin*, 1956, v. 31, 754, 1270 *bis*; 1957, v. 32, 1206.]

S. P. Bedson

IMAGAWA, D. T. & ADAMS, J. M. **Propagation of Measles Virus in Suckling Mice.** *Proc. Soc. Exper. Biol. & Med.* 1958, July, v. 98, No. 3, 567–9. [11 refs.]

Supernatant fluid from HeLa cell cultures infected with the Edmonston strain of measles virus was inoculated intracerebrally into 2 litters of mice aged 1–2 days. 1 mouse showed signs of irritability after 10 days, and the infection could subsequently be carried through 24 brain passages in infant mice; the incubation period ranged from 6 to 12 days, the titre in infant mice from 1·2 to 2·0 log units, and in HeLa cell cultures from 1·5 to 3·2 log units. The virus was still viable after storage at −35°C. for 7 months. It was neutralized in tissue culture by specific human and ferret measles immune sera, and a neutralization test could also be carried out in infant mice. Mouse-adapted virus from the 20th passage produced a characteristic cytopathogenic effect in HeLa cell cultures, but did not appear in the supernatant fluid, and it was necessary to transfer infected cells in order to carry out further passages in tissue culture. *D. J. Bauer*

RUCKLE, Gisela. **Studies with the Monkey-Intra-Nuclear-Inclusion-Agent (MINIA) and Foamy-Agent derived from spontaneously degenerating Monkey Kidney Cultures. I. Isolation and Tissue Culture Behavior of the Agents and Identification of MINIA as closely related to Measles Virus.** *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 2, 139–65, 3 figs. [11 refs.]

Foamy agent appeared alone in 36 cultures grown from 67 pools of rhesus and cynomolgus monkey kidney tissue, and monkey intranuclear inclusion agent (MINIA) appeared alone in 7; they appeared in 13 and 2 respectively of 32 batches of kidneys from individual monkeys. Measles neutralizing antibody was usually absent or present only in low titre in the sera of the monkeys which were infected with MINIA, and a similar relationship was observed with antibody to foamy agent. The cytopathogenic effects produced by the 2 agents could not be reliably distinguished from each other and from those due to measles virus in living cultures. Eosinophilic intranuclear inclusions were found in stained preparations of cultures infected with MINIA but were not seen with foamy agent. In studies carried out in different culture systems MINIA had the same range as measles virus, producing cytopathogenic effects in human amniotic membrane and human kidney, but not in rabbit kidney cultures. Foamy agent and MINIA could be separated by passage in human amniotic membrane, which eliminated foamy

agent, and in rabbit kidney cells, which eliminated MINIA. Titres of 2·4–4·0 log units (ID50 per ml.) were obtained with MINIA and 2·6–3·6 log units with foamy agent. Cross-neutralization and fixation tests with 8 strains of MINIA showed that they were indistinguishable from measles virus. The strains of foamy agent were all antigenically related, and showed no relationship with measles virus or MINIA.

D. J. Bauer

RUCKLE, Gisela. **Studies with the Monkey-Intra-Nuclear-Inclusion-Agent (MINIA) and Foamy-Agent. II. Immunologic and Epidemiologic Observations in Monkeys in a Laboratory Colony.** *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 2, 167–82. [10 refs.]

In a serological examination of normal monkeys arriving at the Virus Research Laboratory, Pittsburgh, in 1955 and 1956, measles antibody was found in 45 of 60 (70%) cynomolgus and 54 of 77 (70%) rhesus monkeys, and antibody to foamy agent in 37 of 57 (65%) and 2 of 22 (9%) of the 2 species respectively. Antibodies to the 2 viruses could not be found in the sera of 8 species of domestic or laboratory animal. 5 monkeys were observed to have become infected with foamy agent during residence in the laboratory for 1 to 3 months. No antibody to MINIA or foamy agent could be found in the sera of 14 persons after vaccination with 2 batches of commercial poliomyelitis vaccine.

D. J. Bauer

GLASGOW, L. A., SANCHIS-BAYARRI, V. & MORGAN, H. R. **Delayed Hypersensitivity** *in vitro.* **III. Effect of Cortisone on Cytotoxicity of Mumps Viral Antigen.** *Proc. Soc. Exper. Biol. & Med.* 1958, July, v. 98, No. 3, 614–17, 5 figs. [22 refs.]

Guineapigs were infected with the Enders strain of mumps virus intranasally and by inoculation into the anterior chamber; 15 of 21 animals thus treated gave a positive reaction to the intradermal injection of mumps skin test antigen. In cultures prepared from fragments of spleen from animals giving a positive skin reaction inhibition of migration of macrophages and progressive cell destruction were observed after infection of the cultures with mumps virus. This cytotoxic effect was greatly reduced by the addition of cortisone acetate in a concentration of 25 μgm. per cc. to the cultures 36 hours before infection. These results suggest that the beneficial effect of corticosteroids in the treatment of mumps orchitis is due to the reduction of hypersensitivity of the tissues to mumps antigen.

[For part II of this series, see this *Bulletin*, 1958, v. 33, 79.] *D. J. Bauer*

BRANDT, C. D. **Inclusion Body Formation with Newcastle Disease and Mumps Viruses in Cultures of Chick Embryo Cells.** *Virology.* New York. 1958, Apr, v. 5, No. 2, 177–91, 6 figs. [33 refs.]

A study has been made of the effect of Newcastle disease and mumps viruses on explants of chorio-allantoic membrane grown in roller tubes. In cultures infected with Newcastle disease virus the extension of cells from the explants was retarded and after 40 hours eosinophil inclusions appeared in the cytoplasm. After 3 days the cells became shrunken and rounded, with pyknotic nuclei and eosinophil cytoplasm. The maximum haemagglutinin titre was attained after 3½ days. The observed effects were all prevented by specific immune serum. Inclusions could only be demonstrated after the use of acid fixatives. In cultures infected with the Enders strain of mumps virus the extension of cells was not inhibited. Eosinophil cytoplasmic inclusions appeared on the second day; no other cytopathogenic effect was produced. Inclusions could not be found in cultures infected with the Lawn strain of mumps virus, or with a number of strains of influenza virus.

D. J. Bauer

FRENCH, E. L. & DINEEN, J. K. **Primary Isolation of Influenza A Virus: the Optimal Conditions for Amniotic Infection.** *Australian J. Exper. Biol. & Med. Sci.* 1958, June, v. 36, Pt. 3, 257–65, 1 fig. [10 refs.]

The use of fertile eggs of different ages for the isolation of Asian influenza virus was investigated. Embryos aged from 13 to 15 days were shown to be more sensitive than 11 day embryos to influenza virus present in throat washings and tracheal swabs [see also this *Bulletin*, 1947, v. 22, 89]. It is recommended that chick embryos 13 to 15 days old should be inoculated intra-amniotically and the amniotic fluid and lung emulsion harvested and tested for haemagglutination after 3 to 5 days' incubation. *H. G. Pereira*

WANG, San-Pin & LIN, Tsu-Yang. **Laboratory Studies on some Biological Properties of the Far East Influenza Virus.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 178–82.

The haemagglutinating properties of 7 strains of Asian influenza virus were compared with those of influenza A, B and C viruses. All Asian and A strains agglutinated human O, guineapig, chicken, mouse, rat, dog, duck and frog erythrocytes. The Asian strains agglutinated, in addition, monkey, sheep, goat, cow, swine, Japanese horse, Chinese pony, rabbit and cat erythrocytes. 2 of 6 type A strains failed to agglutinate monkey erythrocytes. Influenza B (Lee) virus agglutinated all but mouse, sheep, goat, swine, Japanese horse and cat erythrocytes. The only cells agglutinated by influenza C virus were from chicken, mouse, rat and frog.

The Asian strains varied in sensitivity to normal serum inhibitors and 1 strain was particularly sensitive. The highest haemagglutination-inhibition titres were observed in horse and frog sera. Normal serum inhibitors were destroyed by periodate but not by trypsin. *H. G. Pereira*

MOGABGAB, W. J., PELON, W., BURCH, G. E. & HOLMES, Barbara. **Characteristics of the Asian Strain of Influenza A.** *Proc. Soc. Exper. Biol. & Med.* 1958, Oct., v. 99, No. 1, 116–20. [12 refs.]

Growth characteristics, haemagglutinating properties and reactivity with antibody and serum inhibitors were

determined for strains of Asian influenza virus propagated in fertile eggs and in monkey kidney tissue cultures. Virus isolations from throat garglings of patients with Asian influenza were achieved more frequently in eggs inoculated by the amniotic route than in monkey kidney tissue cultures. The amount of virus required to give positive results was 10 to 100 times greater in tissue cultures than in fertile eggs. The haemagglutinating properties of Asian influenza virus strains propagated in tissue culture and in eggs were similar and differed from those of previously isolated viruses in the ability of early passages to agglutinate fowl and sheep erythrocytes. Tissue culture strains were on the whole more sensitive to normal serum inhibitors and to antibody than egg strains. Tissue culture strains are considered superior to egg strains for the detection of haemagglutination-inhibiting and neutralizing antibodies in human convalescent sera.

H. G. Pereira

Cleeland, R. & McKee, A. P. **Antigenic Variation of Asian Influenza Virus.** *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 371–4.

Acute and convalescent sera from 20 patients with Asian influenza were tested by complement-fixation and haemagglutination-inhibition against 20 strains of Asian influenza virus. All serum pairs but one showed 4-fold or higher rises in complement-fixing antibody. According to behaviour in haemagglutination-inhibition tests, the virus strains were divided into 2 groups, the first sensitive and the second insensitive to normal serum inhibitors. The insensitive strains, numbering 12, were tested by haemagglutination-inhibition against the 20 untreated serum pairs and showed wide variations in reactivity with different sera. The possible reasons for this variation are discussed and the suggestion of antigenic differences between strains is favoured by the authors.

The importance of the selection of strains to be used in haemagglutination-inhibition tests is stressed.

H. G. Pereira

Padgett, B. L. & Walker, D. L. **Enzymatic Variants of Influenza Virus. II. Effect of Environmental Factors on Enzymatic Characteristics of a Variant of Influenza B Virus.** *J. Exper. Med.* 1958, Nov. 1, v. 108, No. 5, 651–64, 7 figs.

Enzymatic properties of influenza B (Lee) virus and a previously described variant of the same strain [Padgett *et al.*, this *Bulletin*, 1958, v. 33, 82] were investigated by studying the rate of elution of each virus strain from chicken erythrocytes under different conditions of temperature, *p*H and ionic composition of the suspending medium. The rate of elution of the original strain increased proportionally with temperature between 25°C. and 40°C. whereas the variant strain eluted more rapidly at 25°C. The reduced enzymatic activity of the variant strain at higher temperatures was shown to be due to inhibition rather than inactivation of the enzyme. Elution of the parent strain at 37°C. was not affected by variations in *p*H between 6 and 8 while elution of the variant was decreased at *p*H values above 7. Calcium, strontium and barium ions had a stimulating action on the variant enzyme. The enzymatic behaviour of the variant strain in the presence of sufficient calcium ions, resembled that of the parent strain. Calcium ions were also shown to protect the haemagglutinating and infective properties of the variant against heat inactivation.

H. G. Pereira

Fazekas De St Groth, S. & White, D. O. **The Dose-Response Relationship between Influenza Viruses and the Surviving Allantois.** *J. Hygiene.* 1958, Dec., v. 56, No. 4, 523–34, 2 figs. [16 refs.]

Infectivity titrations of influenza viruses in surviving bits of chick embryo chorio-allantoic membrane were studied with regard to variations in sensitivity and accuracy. Bits of membrane from any one egg showed uniformity of response demonstrated by the Poissonian character of the dose-response curves and by constant haemagglutinin yields. Bits of membranes from different eggs varied in susceptibility and in virus yield but the variations were smaller than those observed with whole eggs. Limitations of the accuracy of infectivity titrations based on quantal responses are discussed and the advantages of the method under study are presented.

H. G. Pereira

Fazekas De St Groth, S. & White, D. O. **Comparison of the Infectivity of Influenza Viruses in Two Host Systems: The Allantois on Intact Eggs and surviving Allantois-on-Shell.** *J. Hygiene.* 1958, Dec., v. 56, No. 4, 535–46. [13 refs.]

A comparative study of influenza virus infectivity titrations performed on surviving bits of chorio-allantoic membrane (tray titrations) and in the allantoic cavity of whole eggs (egg titrations) showed that the average sensitivity of the 2 methods is approximately identical but relative sensitivities expressed as the log tray/egg differences varied, according to virus strain, between + 0·88 (SW strain) and − 1·02 (BON strain). Virus materials with varying infectivity/haemagglutinin ratios gave essentially identical tray/egg infectivity ratios. The difference in sensitivity of the 2 methods of titration was attributed to varying conditions during the intracellular stage of virus multiplication.

H. G. Pereira

Schmidt, B. & Grossgebauer, K. Beobachtungen an Viruserythrocytengemischen in Blutsenkungspipetten. [**Observations on Mixtures of Virus and Red Cells in Sedimentation Tubes**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 144, No. 6, 549–54, 2 figs.

In tests carried out in parallel with conventional haemagglutination titrations a linear relationship has been established between the haemagglutinin titre of allantoic fluids infected with various strains of influenza virus and the logarithm of the time at which the onset of agglutination can be observed in mixtures of red cells and virus drawn up into a sedimentation tube. The same relationship was maintained when the initial haemagglutinin titre of the fluid was reduced to varying

extents by ultraviolet irradiation, dilution, centrifugation, and adsorption and elution. The method enables the titre to be determined within a few minutes without carrying out serial dilutions, and can be carried out equally well with stored red cells treated with formalin.

D. J. Bauer

PELON, W., MOGABGAB, W. J., DIETLEIN, L., BURCH, G. E. & HOLMES, Barbara. **Antibody Response to Asian Influenza Vaccination in Man.** *Proc. Soc. Exper. Biol. & Med.* 1958, Oct., v. 99, No. 1, 120–24.

Monovalent Asian influenza vaccines were administered to volunteers in varying doses as single or multiple injections by intradermal, subcutaneous or intramuscular routes. Antibody response to vaccination was estimated by haemagglutination-inhibition tests performed with tissue culture (TC), egg (E) and egg-ferret-mouse-egg (EFME) lines of Asian influenza virus. Antibody responses to vaccination by different routes were essentially identical and varied directly with the total volume of vaccine administered either as a single dose or in 2 doses spaced by 3 weeks.

Haemagglutination-inhibition titres of post-vaccination sera varied according to the virus line used in the test. The titres obtained were lower with the E line than with the TC or EFME lines. The same was not the case with sera of patients convalescing from natural disease which reacted better with the TC line than with either the E or EFME lines.

The importance of the selection of virus strains for use in the serological evaluation of influenza vaccines is discussed. *H. G. Pereira*

MATUMOTO, M., UCHIDA, S., HOSHIKA, T. & MATSUYAMA, T. **Isolation of an Intermediate Type of Adenovirus from a Fatal Case of Infantile Pneumonia.** *Japanese J. Exper. Med.* 1958, Aug., v. 28, No. 4, 305–15. [30 refs.]

An agent belonging to the adenovirus group (Takeuchi strain) was isolated from different parts of lung tissue from a fatal case of pneumonia in a 3-month-old infant. Identification of the agent as adenovirus was based on cultural and serological properties, ether resistance and failure to multiply in laboratory animals or in fertile eggs. A rabbit antiserum prepared with the Takeuchi strain was tested by serum neutralization against adenovirus types 1 to 14 giving positive reactions with types 3 and 7. Cross neutralization tests between the new virus and adenovirus prototypes 3 and 7 gave the following results:

	Virus		
Rabbit immune serum	Type 3	Type 7	Takeuchi strain
Type 3	512	4	64
Type 7	4	128	64
Takeuchi strain	256	256	512

The same behaviour was observed with virus materials obtained after serial passage of the Takeuchi strain in HeLa cell cultures containing type 3 or type 7 antiserum. The possibility of a virus mixture is considered to be unlikely and it is suggested that the Takeuchi strain has double serological pattern of adenovirus types 3 and 7. *H. G. Pereira*

GEORGIADES, J. & CICHOLSKA, Aniela. **Cytopathological Changes in the Tissue Detroit-6 infected with Viruses of the APC Group.** Report I. *Bull. Inst. Marine Med. Gdańsk.* 1958, v. 9, Nos. 3/4, 103–9, 3 figs. [23 refs.]

GEORGIADES, J. **Cultivation of APC Viruses on the Tissue Detroit-6.** *Bull. Inst. Marine Med. Gdańsk.* 1958, v. 9, Nos. 3/4, 111–15.

LENNETTE, E. H., FOX, Virginia L., SCHMIDT, Nathalie J. & CULVER, J. O. **The Coe Virus: an apparently New Virus recovered from Patients with Mild Respiratory Disease.** *Amer. J. Hyg.* 1958, Nov., v. 68, No. 3, 272–87, 1 fig. [17 refs.]

A cytopathic agent, designated Coe virus, was isolated from the throat washings of 4 patients with respiratory infections diagnosed as pharyngitis (3 patients) and common cold. The virus was isolated in HeLa cell cultures where it caused cytopathic effect starting at 6 days' incubation on primary cultivation and at shorter times in subsequent passages. Tissue culture materials gave infectivity titres in HeLa cell cultures reaching levels between 10^{-5} and 10^{-6}. The cytopathic effect of all 4 strains could also be demonstrated in cultures of KB cells, FL human amnion cells and in embryonic rabbit kidney cells but not in monkey kidney cells. Cytopathic changes consisted of rounding of the cells, granulation of the cytoplasm, loss of nuclear outline and eventual cell fragmentation and detachment. The virus could not be propagated in fertile eggs or in adult or newborn mice but showed slight pathogenicity for the last. No haemagglutinins for human or chicken erythrocytes could be detected in infected tissue culture fluids. A complement-fixing antigen reacting with human convalescent sera was demonstrated and tentatively correlated with the virus particles. Serum neutralization tests performed in HeLa cell cultures with sera from patients and from immunized animals showed the identity of the strains isolated from each of the 4 patients and distinguished the Coe virus from herpes simplex virus, poliovirus Types 1 to 3, adenovirus types 1 to 8, Coxsackie A types 1 to 19, Coxsackie B types 1 to 5, ECHO types 1 to 19 and respiratory syncytial virus.

Acute and convalescent sera from 3 of the 4 patients (no convalescent serum from the remaining patient was available) showed rises in serum neutralizing and complement-fixing antibodies for the Coe virus. Paired sera from another group of patients with respiratory disease showed serum-neutralizing antibody rises for the Coe virus in 5 out of 23 cases.

The authors cautiously conclude that the Coe virus may be associated with human respiratory disease.

H. G. Pereira

DUBREUIL, R. & PAVILANIS, V. Emploi d'un milieu synthétique simplifié pour la culture *in vitro* de cellules animales et du virus de la poliomyélite. **[Use of a Simplified Synthetic Medium for *in vitro* Cultivation of Animal Cells and Poliomyelitis Virus]** *Canadian J. Microbiol.* Ottawa. 1958, Oct., v. 4, No. 5, 543–50. [14 refs.]

The most commonly used synthetic medium for the propagation of poliovirus in tissue culture, and that almost universally used for the preparation of poliovaccines, is medium 199 of MORGAN, MORTON and PARKER (*Proc. Soc. Exper. Biol. & Med.*, 1950, v. 73, 1). It is now clear that this medium is more complicated than is required for the production of poliovirus, indeed EAGLE and HABEL [this *Bulletin*, 1956, v. 37, 1270] found that the yield of poliovirus is as great in a simple salt solution with glucose and glutamine as it is in more complete media. The authors describe a medium consisting of Hanks solution with glucose (2 gm. per litre) *d*-ribose, *l*-cysteine and *l*-glutamine. This medium has been successfully used as a maintenance medium for established monkey kidney cultures. When supplemented with serum it is adequate for the establishment of such cultures or the propagation of HeLa cells. The yield of poliovirus and the quality of poliovaccine derived therefrom is as good as that prepared with more complex media. *A. J. Beale*

LIKAR, M. & WILSON, D. C. **Observations on the Interaction of Poliovirus and Host Cells *in vitro*: 1. The Effect of Environmental Temperature.** *Brit. J. Exper. Path.* 1958, Dec., v. 39, No. 6, 674–8, 5 figs. (3 on pl.) [11 refs.]

A study was made of the yield of Type 1 poliovirus (Mahoney strain) grown in monkey kidney monolayer cultures held at various temperatures. The temperatures studied were 4, 20, 30, 37, 39, 39·5 and 40·5°C. It was found that virus multiplied at all these temperatures but the yield was low at low temperatures rising to a maximum at 39·5°C. Cultures held at 40·5°C. gave about a 1,000-fold lower yield than cells maintained at 39·5°C. and also these cells failed to show any cytopathic effects of the virus growth. If cells which had been maintained and infected at 40·5°C. were subsequently released from the glass with versene and subcultured into fresh tubes one-half of which were maintained at 40·5°C. and one-half at 37°C. it was found that the cells maintained at 40·5°C. failed to show any cytopathic effects and grew well while cells that were maintained at 37°C. showed the usual cytopathic effects of poliovirus infection. *A. J. Beale*

MANDEL, B. **Studies on the Interactions of Poliomyelitis Virus, Antibody, and Host Cells in a Tissue Culture System.** *Virology.* New York. 1958, Oct., v. 6, No. 2, 424–47, 9 figs.

The introduction of tissue culture technique into animal virology has added precision to studies of virus neutralization. This paper reports ingenious studies on the neutralization of poliovirus Type 1, with HeLa cells as the assay system. The general plan of these experiments was to add virus or virus treated for a period with antiserum to HeLa cells. A time (usually 1 hour) was allowed for adsorption and then the cultures were washed. Various treatments were then given, either the cultures were immediately overlaid with agar, or allowed to stand in fluid medium before agar overlaying or given a second treatment with antiserum washed and then overlaid.

By these methods it was established that free virus at 37°C. rapidly adsorbs to the cells and disappears beyond the influence of antiserum. Virus antiserum complexes adsorb to the cell without infecting it, but tend to dissociate, so that a second antiserum treatment reduces the count compared with a single treatment. Exposure to a low *p*H (6, or lower) caused more rapid dissociation of antibody-virus complexes. It was found that the number of plaques was less if the agar overlay was added immediately, but the cause for this was not discovered. Since a similar effect was noted with a plasma clot overlay it was thought to be a function of the physical state.

The observations of DULBECCO *et al.* [this *Bulletin*, 1956, v. 31, 959] that there is constant fraction surviving even excess antiserum treatment were confirmed. It was found that by a second treatment with antiserum these survivors could be reduced up to 10-fold.

A. J. Beale

BINN, L. N. & HILLEMAN, M. R. **Detection of Poliovirus I in Monkey Kidney Cultures inoculated with Overwhelming Dose of Adenovirus 4.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 127–8.

When preparing adenovirus or other viral vaccines in monkey kidney tissue cultures the possibility that they may be contaminated with polioviruses has to be borne in mind. An experiment is described which shows that poliovirus Type 1 can be detected as readily when passed in the presence of 1,000 tissue culture doses of adenovirus type 4 adapted to grow on monkey kidney cells as when passed in monkey kidney tissue alone. With doses of poliovirus between 0·4 and 40 TCD50 the cytopathic changes in monkey kidney cells also infected with adenovirus were predominantly of the adenovirus type. Subculture into tubes containing adenovirus type 4 antiserum revealed that poliovirus Type 1 had in fact multiplied in the monkey kidney tissue. The authors therefore recommend that the safety test of viral vaccines for poliovirus should be carried out on the living virus before inactivation. It is well known that after partial inactivation with formaldehyde exhaustive tests are required to reveal poliovirus. *A. J. Beale*

SCHMIDT, Nathalie J. & LENNETTE, E. H., with the technical assistance of Jessie H. DOLEMAN, Shirley J. HAGENS & Juanita DENNIS. **The Behaviour of Different Strains of Poliomyelitis Virus in the Complement Fixation Reaction. I. Comparison of Sensitivity of Antigens derived from Laboratory Strains and Patient's Own Infecting Strain.** *J. Immunology.* 1958, Oct., v. 81, No. 4, 309–16. [12 refs.]

Complement-fixation tests were done on sera from poliomyelitis patients, with laboratory strains of polio-

virus and the strain isolated from the patient. The stock strains used were Mahoney Type 1, Statler Type 2 and McMullen Type 3. Sera from 21 patients who were ill in 1952, 1953, or 1954 were studied (Type 1, 15; Type 2, 1 and Type 3, 5). It was found that there were only insignificant differences in the titres obtained with the patients' own virus or the standard strain. Similarly there was very little difference in the time of appearance or duration of the antibodies. The authors therefore conclude that the antigenic structure detectable by complement-fixation is similar within the 3 main serological types of poliovirus. This means that stock laboratory strains can be used as diagnostic reagents. However, with one exception when there were differences, the highest titre was obtained with the strain isolated from the patient. In 1 patient a serological diagnosis could only be made with the homologous strain, and in 3 others the diagnosis could be made earlier. On the other hand, 3 patients failed to show a diagnostic (4-fold) rise in antibody titre with either antigen. *A. J. Beale*

ROIZMAN, B., MAYER, M. M. & RAPP, H. J. **Immunochemical Studies of Poliovirus. III. Further Studies on the Immunologic and Physical Properties of Poliovirus Particles produced in Tissue Culture.** *J. Immunology*. 1958, Nov., v. 81, No. 5, 419–25, 1 fig. [10 refs.]

This paper describes work showing that there are 4 sorts of particles having virus activity in tissue culture fluid infected with poliovirus. All the particles react in complement-fixation [CF] tests with sera drawn from individuals infected with poliovirus. They are distinguished according to whether they are infectious or not by their sedimentation constant, and by their reactivity in CF tests. A system of nomenclature which is proposed together with some of the characters of these particles is shown in the Table.

Nomenclature of poliovirus particles and their properties

Particle Designation	Biologic Property	Sedimentation Constant	Antigenic Reactivity	Other Properties
ID+	Infectious	160 Svedberg units	D	Uniformly spherical
NID+	Non-infectious	Homogeneous	D	25–30% nucleic acid
NID−	Non-infectious	80–90 Svedberg units	D	Lack nucleic acids
NIC−	Non-infectious	Non-homogeneous	C	Flatter, less uniform and less sharply delineated than the ID+ and NID+ particles

In this nomenclature I stands for infectious and NI for non-infectious. C and D for reactivity in complement-fixation tests. Thus C antigen reacts with acute sera (most acute sera have some anti D also but a few pure anti C sera do occur) and D antigen with convalescent poliomyelitis sera. The + sign means that the sedimentation constant is high, about 160 S, and − that it is low, about 80–90 S. D antigen content is constantly related to the number of poliovirus particles visible in the electron microscope. The relationship is 1D CF unit to 10^{10} particles. It seems likely that NID+ particles are derived from ID+ by degradation. Similarly inactivation may lead in series through NID− to NIC−. It is, however, possible that these incomplete virus particles are stages in the course of virus reproduction, but as yet there is little evidence for this suggestion.

[For Part II in this series, see this *Bulletin*, 1958, v. 33, 1094.] *A. J. Beale*

ROMANO, E. Dosaggio della formaldeide nel vaccino antipoliomielitico. [**Determination of Formaldehyde in Poliomyelitis Vaccine**] *Riv. Istituto Sieroterap. Ital.* 1958, May–June, v. 33, No. 3, 145–9. English summary (5 lines)

An examination has been made of the accuracy of the titration of formaldehyde by the MacFadyean method, which is based on the formation of a coloured product with chromotropic acid. 10 replicate estimations carried out on a 1 : 4,000 dilution of formalin gave a mean value of 91·65 ± 0·85 mgm. per litre, and 8 replicate determinations on a sample of poliomyelitis vaccine gave a mean value of 74·00 ± 1·07 mgm. per litre. Titration of formalin diluted in medium 199 gave results very close to the expected values, but determinations of bound formaldehyde carried out on vaccine neutralized with sodium bisulphite gave low values. This error could be avoided by diluting the sample after incubation with dimedone, instead of before incubation as in the standard technique. *D. J. Bauer*

DALLDORF, G. & WEIGAND, H **Poliomyelitis as a Complex Infection.** *J. Exper. Med.* 1958, Nov. 1, v. 108, No. 5, 605–16, 3 figs. [26 refs.]

Coxsackie A and polioviruses are often epidemiologically associated. There is increasing suspicion that some of the Coxsackie A strains may cause central nervous system lesions in man. At least 2 types (Coxsackie A7 and 14) have been shown to cause poliomyelitis-like lesions in monkeys [HABEL and LOOMIS; DALLDORF, this *Bulletin*, 1958, v. 33, 999]. Dalldorf now reports experiments suggesting that 2 (Coxsackie A and attenuated poliovirus) viruses each able to produce subclinical neuronal lesions may if given successively produce clinical disease by an additive effect.

The viruses used were Coxsackie A14 and an attenuated poliovirus Type 1 ("80–4" No. 5733 obtained from SABIN) inoculated for most of the experiments used into young cynomolgus monkeys. It was established that neither strain alone caused paralysis by combined intracerebral and intramuscular inoculation and that a second dose of the same virus also did not cause paralysis. When both viruses were given simultaneously

none of 5 animals was paralysed. However in 3 experiments involving 18 animals poliovirus was given 5 days before Coxsackie A14 and 12 animals became paralysed. 2 out of 3 animals were paralysed when the Coxsackie A14 inoculation was delayed for 25 days. The severity of the histological lesions was also increased by administering both viruses at an interval of 5 days.

Similar experiments were done with Coxsackie A7 and the attenuated poliovirus strain. 2 out of 5 animals (1 of these was a rhesus monkey as were 2 of the control monkeys used) given poliovirus as before and Coxsackie A7 intramuscularly 5 days later became paralysed. The histological lesions again were more severe in the successively infected animals.

Although cautious in jumping to conclusions about the implications for human infections Dalldorf does suggest that human paralytic poliomyelitis may sometimes be a complex infection summating the effects of 2 viruses and thus causing more severe disease.

A. J. Beale

Sommerville, R. G., McIntosh, E. G. S. & Carson, H. G. **The Growth Cycle of ECHO Viruses in Tissue Culture: I. Maturation and Release of ECHO Virus Types 1, 2, 7 and 11, from Monolayer Cultures of Monkey Kidney Cells.** *Brit. J. Exper. Path.* 1958, Dec., v. 39, No. 6, 589–96, 4 figs.

Hsiung and Melnick [this *Bulletin*, 1957, v. 32, 1204] have divided the ECHO viruses into 4 groups based on the character and speed of appearance of the plaques produced in rhesus monkey kidney cells. In this work 4 ECHO viruses, types 1, 2, 7 and 11, a representative of each of the 4 plaque forming groups were studied in growth cycle experiments. Titrations were made of the free virus in the tissue culture fluid and also of the cell associated virus. The time of first appearance of new virus, the average maturation time (defined by Howes and Melnick, *Virology*, 1957, v. 4, 97 [this *Bulletin*, 1958, v. 33, 996] as "the time elapsing between inoculation and the appearance of 50% of the total mature (infectious) virus produced by the cells") and the average yield of infectious virus per cell were recorded. As with poliomyelitis virus it was found that the proportion of free virus at the average maturation time was only a few per cent of the total virus in the culture. The maturation times were about 3 hours for ECHO 1 and about 7 hours for the other 3 types of virus. No definite correlation could be made between the characters measured by the growth cycle experiments and the characters used to divide them into plaque forming groups. It was found that with the exception of ECHO 1 the size of the plaque was inversely related to the number of infectious virus particles that were produced per cell. Thus ECHO 2 virus produced 496 infectious units per cell but produced no plaques at all, whereas ECHO 11 produced 142 infectious units per cell and the plaque size was 1·5 to 2 millimetres at 13 days, whereas ECHO 7 produced 59 infectious units per cell and the plaques were 11·4 millimetres in diameter at 10 days.

On the other hand, ECHO 1 virus produced plaques of 5·6 millimetres diameter at 10 days but only 0·34 of an infectious unit per cell. In the growth cycle experiments for ECHO 1 it was found that the level of infectivity in the tissue culture fluid fluctuated sharply suggesting that virus after its release into the fluid was rapidly re-adsorbed to fresh cells. The proportion of free virus in these cultures was, however, 1·2% which was not as low as that found with ECHO 7 virus when only 0·08% of the virus present in the cultures was free in the fluid. *A. J. Beale*

Drouhet, Victoria, with the technical collaboration of Henriette Goareguer. Sur l'effet cytopathogène du virus ECHO 10. [**The Cytopathogenic Effect of ECHO Virus Type 10**] *Ann. Inst. Pasteur.* 1958, Dec., v. 95, No. 6, 781–4, 2 figs. on pl. [12 refs.]

The English summary appended to the paper is as follows:—

"ECHO virus type 10 has been isolated from children's stools on cultures of *Erythrocebus patas* epithelial cells. On these cultures, the virus induces a cytopathogenic effect, producing very large cytoplasmic inclusion bodies, which differentiates it from the other ECHO viruses known to-day."

Eggers, H. J. Quantitative Untersuchungen zur Komplementbindungsreaktion bei der lymphozytären Choriomeningitis. [**Quantitative Studies of the Complement-Fixation Test with Lymphocytic Choriomeningitis Virus**] *Arch. f.d. gesamte Virusforschung.* 1958, v. 8, No. 2, 221–9, 1 fig. [20 refs.]

A quantitative study has been made of the complement-fixation test with lymphocytic choriomeningitis virus, with guineapig lung suspension as S antigen and determination of the 50% haemolysis end point with a photoelectric absorptiometer. Antiserum dilutions were made in veronal buffer up to 1 : 5 and thereafter in 20% horse serum in order to maintain a relatively constant protein content. Fixation was carried out for 16–18 hours at 4°C. 3 human convalescent-phase sera were titrated over a range of dilutions and with several dilutions of antigen; the number of units of complement fixed showed a linear relation against serum dilution over a wide range provided that the optimal concentration of antigen was chosen. *D. J. Bauer*

Clarke, D. H. & Casals, J. **Techniques for Hemagglutination-Inhibition with Arthropod-Borne Viruses.** *Amer. J. Trop. Med. & Hyg.* 1958, Sept., v. 7, No. 5, 561–73. [17 refs.]

This paper cannot be satisfactorily abstracted as it is a detailed account of the techniques employed at the Rockefeller Foundation Virus Laboratories. 3 methods of antigen production are described and recommendations for their use in a wide variety of arboviruses are tabulated: acetone-ether extraction, sucrose-acetone extraction, and alkaline aqueous extraction. The techniques of haemagglutination and haemagglutinin-inhibition are described including the preparation of sera for testing. A method for storing the goose-cells used is also detailed. This paper should be read in full. *C. E. Gordon Smith*

BLASKOVIC, D. **Natural Foci of Equine Encephalomyelitis in Czechoslovakia. An Announcement.** *Acta Virologica.* Prague. 1958, July–Sept., v. 2, No. 3, 198–200.

This is an explanation that a strain of eastern equine encephalomyelitis and a strain of western equine encephalomyelitis viruses which were obtained from the United States in 1947 were interchanged at the Institute of Virology of the Czechoslovak Academy of Sciences so that work based on these led to the identification of a strain of eastern equine virus isolated by BÁRDOS [this *Bulletin,* 1959, v. 34, 178] as western equine. The confusion was revealed when this virus was studied by PORTERFIELD in London. The strains of eastern and western viruses were apparently not mixed in any way but merely had their names interchanged. A list is given of 17 papers which require correction as a result of this confusion.

C. E. Gordon Smith

ŘEHÁCEK, J. **Elimination of the Virus of Eastern Equine Encephalomyelitis (EEE) in the Faeces of experimentally infected Ticks** *Ixodes ricinus* **L. and** *Dermacentor marginatus* **Sulz.** *Acta Virologica.* Prague. 1958, July–Sept., v. 2, No. 3, 158–63, 2 figs. [20 refs.]

Laboratory reared ticks and a strain of eastern equine virus isolated from *Clethrionomys glareolus* in E. Slovakia were used. Ticks were allowed to start feeding on a mouse which was then inoculated intracerebrally with virus. Virus was isolated from the faeces of larvae, nymphs, and adults of *Ixodes ricinus* and from nymphs and adults of *Dermacentor marginatus.* The titre of virus in the faeces was 10^{-1} to 10^{-4} and persisted in *I. ricinus* for 8–11 days. Mice were not successfully infected by inhalation of faeces but their application to scarified skin produced antibody formation although no symptoms. Oral administration of faeces to suckling mice caused deaths [at the second passage].

C. E. Gordon Smith

GRESÍKOVÁ, M., with the technical assistance of A. STYKOVÁ. **Excretion of the Tick-Borne Encephalitis Virus in the Milk of Subcutaneously Infected Cows.** *Acta Virologica.* Prague. 1958, July–Sept., v. 2, No. 3, 188–92, 3 figs.

Subcutaneous inoculation of the Hypr strain of virus caused no illness in the cows apart from a slight fever. Virus was found in the blood 1–4 days after infection and in the milk 2–6 days after infection. In 2 of the 3 animals, viraemia preceded the virus in the milk. Neutralizing antibodies were found in the cows' sera 1–2 months after infection.

C. E. Gordon Smith

BENDA, R. **The Common Tick,** *Ixodes ricinus* **L. as a Reservoir and Vector of Tick-Borne Encephalitis. I. Survival of the Virus (Strain B3) during the development of the Tick under Laboratory Conditions.** *J. Hyg, Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 3, 314–30, 4 figs. [31 refs.]

II. Experimental Transmission of Encephalitis to Laboratory Animals by Ticks at Various Stages of Development. *Ibid.,* 331–44, 6 figs. [22 refs.]

i. Larvae of *I. ricinus* were infected by feeding on viraemic mice, and nymphs bred from them contained 2·0–5·8 log LD50 of virus 4–6 weeks later. A series of nymphs were next infected by feeding and the resultant imagos contained 4·5–7·5 log LD50 of virus after 5–12 weeks. In different groups the proportion of imagos infected was 16/26, 15/20, 21/26 and 20/22. 62 adult females were fed on infected animals for 3–5 days and 14 of them produced infected eggs: larvae from the eggs of 4 of them were infected. Of 14 similar females fed on infected animals for 7–10 days 3 produced infected larvae. Benda estimates that in nature 10% of infected females produce infected larvae. Transmission to mice was achieved with the larvae from infected females. In a final experiment the infection was shown to persist from infected larvae through nymph to imago regardless of whether the ticks were fed on immune or non-immune animals. Titres of virus did, however, appear to be higher in those fed on non-immune animals and this may have been due to re-infections as non-immune animals circulate virus while the ticks are feeding. In ticks hibernating at 4°C. no change in pathogenicity of the virus was detected [no evidence is given in support of the statement that there was also no antigenic change in the virus].

ii. Infected larvae fatally infected mice by bite although not all infected batches of larvae were able to transmit. During the feeding of ticks on an animal which subsequently died there was always circulation of virus. Larvae were also found to be able to confer immunizing doses of virus and no viraemia was detected during such infections. The faeces of infected larvae contain virus even when they have fed on immune animals. Nymphs transmitted larger doses of virus but did not cause viraemia in immune animals. Nymph faeces were highly infective and unaffected by feeding on immune animals. Adult ticks transmitted even larger doses than nymphs, causing fatal infection even in 3 of 7 mice with protection indices of over 17,000 although there was prolongation of the incubation period compared with non-immune mice. Faeces of adult ticks fed on immune animals had much less virus than those fed on non-immune animals. Antibody increases in guineapigs occurred only when virus circulated during feeding of the infected ticks. Subcutaneous inoculation of guineapigs and rabbits (for which the virus is non-pathogenic) gave earlier circulation of virus and earlier antibody formation than tick infections. In such non-susceptible animals viraemia persists only so long as the ticks are feeding—cross-infection between ticks may, however, occur in this way.

C. E. Gordon Smith

WELSH, H. H., NEFF, Beverley J. & LENNETTE, E. H. **The Isolation and Identification of Turlock Virus in Tissue Culture.** *Amer. J. Trop Med. & Hyg.* 1958, Sept., v. 7, No. 5, 536–42. [10 refs.]

Turlock virus has been isolated repeatedly from *Culex tarsalis* in California [this *Bulletin,* 1958, v. 33,

624]. This paper describes its isolation and identification in chick embryo tissue cultures similar to those used for western equine encephalomyelitis virus [this *Bulletin*, 1958, v. 33, 894]. Non-specific cytotoxicity was present in about one-third of the mosquito suspensions. 5 of the 9 strains isolated were established by the second passage and the remainder at the third passage; a further passage of the negative materials failed to reveal further strains. At second passage 4 of the strains required more than 4 but not more than 7 days for almost complete cell destruction in the cultures—much longer than western equine virus. Comparison with mice and embryonated eggs suggested that tissue culture was at least as sensitive. Identification of the strains was by a neutralization test with a single dilution of antiserum (capable of neutralizing 5 log of stock virus) and a single dilution of unknown virus (based on an estimate of the concentration of virus in fresh isolates). *C. E. Gordon Smith*

LAVILLAUREIX, J., VERMEIL, C. & PETROVIC, A. Pouvoir pathogène expérimental du virus West Nile pour la gerbille et pour la souris blanche. [**Pathogenicity of West Nile Virus for Gerbils and White Mice**] *C.R. Soc. Biol.* 1958, v. 152, No. 6, 1007–9.

West Nile virus [strain not described] was inoculated into albino mice and gerbils (*Gerbillus hirtipes*). In first passage [apparently intracerebral] in the gerbils only inapparent infections with the production of neutralizing antibodies were caused. After 1 blind passage of the brain of an infected gerbil on the 4th day after inoculation fatal encephalitis was produced in gerbils. In both mice and gerbils the incubation period was 4–7 days: excitement and tremors were followed by paralysis and coma. The total duration of symptoms did not exceed 48 hours. The histological changes found in the central nervous system of mice and gerbils are described but do not differ from other descriptions of encephalitis caused by encephalitic viruses in mice. *C. E. Gordon Smith*

TIKHONENKO, T. I. & BORODINA, T. A. **Composition and Content of Nucleic Acids in the Brain of White Mice infected by Japanese B and Tick-Borne Encephalitis Viruses.** *Acta Virologica.* Prague. 1958, July–Sept., v. 2, No. 3, 152–7, 1 fig. [20 refs.]

Mice were infected intracerebrally with Japanese B and tick-borne encephalitis viruses and control mice were inoculated with normal brain. The brain material was subjected to extraction with trichloracetic acid, followed by alkaline hydrolysis. The composition of the nucleic acids was estimated by paper chromatography and their amount determined spectrophotometrically. The nucleotide composition of the RNA and DNA in infected brains did not differ from normal brain. Infected brains showed an increase in RNA of about 10%, compared with the control, 1 day after infection, and of about 20% 3 days after infection; there was no further increase at the fourth day. DNA increased more slowly in infected brains to about 5% more than the control, 1 day after infection, to about 20% more than the control 3 days after infection, and to 26–30% more than the control 4 days after infection. There was little if any difference between the 2 viruses. *C. E. Gordon Smith*

MÖBEST, H. Ein experimenteller Hinweis zur Frage der Temperaturempfindlichkeit des Virus fixe Pitman-Moore. [**Experimental Findings on the Sensitivity of Fixed Virus (Pitman-Moore) to Temperature**] *Arch. f. Hyg. u. Bakt.* 1958, Dec., v. 142, No. 8, 581–7. [11 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 433.]

STARKE, G. & SEIDL, S. Experimentelle Untersuchungen zur Frage der Hämagglutination des Tollwutvirus. [**Experimental Investigations on the Possibility of Haemagglutination by Rabies Virus**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Jan.–Feb.–March–Apr., v. 4, Nos. 1/2, 118–23. [11 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 433.]

HALLAUER, C. & MEYER, K. F. [Edited by.] Handbuch der Virusforschung. [**Handbook of Virus Research**] Vol. IV, pp. xv + 688, 61 figs. 1958. Vienna 1: Springer-Verlag, Mölkerbastei 5. [£12.11.6.]

This book was reviewed on p. 183.

RHODES, A. J. [M.D., F.R.C.P., F.R.S.C.] & VAN ROOYEN, C. E. [M.D., D.Sc., M.R.C.P., F.R.C.P.] **Textbook of Virology for Students and Practitioners of Medicine.** 3rd Edition, pp. xv + 642, 81 figs. 1958. London: Baillière, Tindall & Cox, Ltd. 7 & 8, Henrietta Street, W.C.2. [80s.]

This book was reviewed on p. 182.

IMMUNITY

BURNET, F. M. **A Modification of Jerne's Theory of Antibody Production using the Concept of Clonal Selection.** *Australian J. Sci.* 1957, Oct. 21, v. 20, No. 3, 67–9.

The hypothesis is stated as follows:—

"The plasma γ-globulins comprise a wide variety of individually patterned molecules and probably several types of physically distinct structure. Amongst them are molecules with reactive sites which can correspond probably with varying degrees of precision to all, or virtually all, the antigenic determinants that occur in biological material other than that characteristic of the body itself. Each type of pattern is a specific product of a clone of mesenchymal cells and it is the essence of the hypothesis that each cell automatically has available on its surface representative reactive sites

equivalent to those of the globulin they produce. For the sake of ease of exposition these cells will be referred to as lymphocytes, it being understood that other mesenchymal types may also be involved. Under appropriate conditions, cells of most clones can either liberate soluble antibody or give rise to descendant cells which can.

"It is assumed that when an antigen enters the blood or tissue fluids it will attach to the surface of any lymphocyte carrying reactive sites which correspond to one of its antigenic determinants. The capacity of a circulating lymphocyte to pass to tissue sites and there to initiate proliferation is now relatively well established (cf. Gowens, 1957; Simonsen, 1957). It is postulated that when antigen-natural antibody contact takes place on the surface of a lymphocyte the cell is activated to settle in an appropriate tissue, spleen, lymphnode or local inflammatory accumulation, and there undergo proliferation to produce a variety of descendants. In this way preferential proliferation will be initiated of all those clones whose reactive sites correspond to the antigenic determinants on the antigen used. The descendants will include plasmacytoid forms capable of active liberation of soluble antibody and lymphocytes which can fulfil the same functions as the parental forms. The nett result will be a change in the composition of the globulin molecule population to give an excess of molecules capable of reacting with the antigen, in other words the serum will now take on the qualities of specific antibody. The increase in the number of circulating lymphocytes of the clones concerned will also ensure that the response to a subsequent entry of the same antigen will be extensive and rapid, i.e. a secondary type immunological response will occur."

NOSSAL, G. J. V. **Antibody Production by Single Cells.** *Brit. J. Exper. Path.* 1958, Oct., v. 39, No. 5, 544–51, 2 figs. [15 refs.]

A single-cell technique for the study of antibody production *in vitro* is described in detail. Of 416 single cells from the lymph nodes of rats immunized against *Salmonella typhi* or Salm. Adelaide or both 56 formed sufficient antiflagellar antibody in 4 hours to immobilize small numbers of bacteria. The amount of antibody produced by these active cells was fairly constant from cell to cell and was not increased by the addition of feeder cells.

When droplets containing varying numbers of lymph node cells were used, the percentage of positive droplets was directly proportional to the number of cells present showing that inactive cells were not producing sub-threshold amounts of antibody.

326 single cells from animals immunized with both antigens were tested and no cell was found to produce antibodies against both antigens. This finding is in agreement with BURNET'S [see above] clonal selection hypothesis of antibody formation, though the author points out that in the present experiment only the current phenotype of the cell is being tested and there is no direct evidence of true genotypic restriction.

Sheila McDonald

STAVITSKY, A. B. *In vitro* **Production of Diphtheria Antitoxin by Tissues of Immunized Animals. III. Incorporation of Amino Acids into Antibody; Relationship to Antibody Synthesis and Sensitivity Relative to other Methods.** *Brit. J. Exper. Path.* 1958, Dec., v. 39, No. 6, 661–73. [Numerous refs.]

SAHA, K. & CHAUDHURI, S. N. **Studies on the Nature of Antigen-Antibody Reaction. Part I. Spectrophotometric Study of Hapten-Antiserum Reaction.** *Ann. Biochem. & Exper. Med.* 1958, v. 18, No. 3, 89–94, 2 figs. [11 refs.]

WALTON, K. W. & ELLIS, H. A. **A Method for Serial Determinations of Serum Complement.** *Immunology.* Oxford. 1958, July, v. 1, No. 3, 224–33, 4 figs. [18 refs.]

This paper gives an account of some of the difficulties involved in finding a reliable and reproducible method of determining serum complement; it describes a method which overcomes these difficulties. Complement is estimated by mixing serial dilutions of serum with a standardized suspension of sensitized sheep red cells. The concentration of serum giving 50% haemolysis is found by the use of a design which relates the probit per cent haemolysis to the reciprocal of the corresponding serum dilution. The degree of haemolysis is estimated by measuring spectrophotometrically the haemoglobin in the supernatant from the partially lysed cells.

The most important source of error in complement determinations arises from the use of different batches of formolized sheep red cells. This is overcome by running a lyophilized standard reference serum in parallel with all titrations and correcting the values found for the unknown sera in accordance with the value obtained for the reference serum for any particular batch of sheep red cells. *R. B. Morrison*

BRAMBELL, F. W. R. **The Passive Immunity of the Young Mammal.** *Biol. Reviews.* 1958, Nov., v. 33, No. 4, 488–531, 11 figs. [Numerous refs.]

This review is based on a course of 4 lectures given in King's College, University of London, in November 1957. In addition to a comprehensive survey of the subject, it includes an account of the considerable amount of work carried out by the author and his colleagues of the Agricultural Research Council Unit of Embryology.

It consists of 5 sections beginning with an introduction in which are discussed the nature and production of antibodies, transmission of passive immunity to the young, immunological incompatibility and haemolytic disease, and transport of large molecules. The remaining 4 sections deal with uterine immunity, transmission of immunity before birth, transmission of immunity after birth, and selective transport of proteins by the endoderm. *R. B. Morrison*

BRAUNE, J. F. Über die Auslösung von Anaphylaxie-Erscheinungen bei Meerschweinchen durch präzipitierende Antikörper. V. und Schlussmitteilung. Vergleichende Untersuchungen zwischen Präzipitations-optimum und Schockoptimum. [**Anaphylaxis in Guineapigs provoked by Precipitating Antibodies. V. and closing communication**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 107–15. [13 refs.]

The purpose of this work is to throw light on the varying theories of allergy and anaphylaxis by studying the capacity of antigen/antibody mixtures prepared *in vitro* to determine the phenomenon of anaphylaxis when injected to the guineapig.

The outcome of these investigations is to show that the phenomenon of anaphylaxis can be obtained by injection of a suitable mixture of antigen and antibody. It is essential, however, for this purpose, that the antigen should be present in excess and when a graded range of antibody/antigen mixtures is prepared, the ratio of antibody to antigen is much higher for optimum precipitation than for shock production.

A gradation in the following order is obtained when progressively more antibody is added to antigen:—antigen excess—optimal mixture for shock production—zone of maximal precipitation—zone of most rapid precipitation—zone of maximal complement-fixation—antibody excess. *J. W. McLeod*

Book Reviews

CIFERRI, R. & REDAELLI, P. **Bibliographia Mycopathologica (1800–1940). II.** 399 pp. 1958. Florence: Sansoni Antiquariato. (Biblioteca Bibliographia Italica No. 20.) [L. 30,000 for the set.]

This second (and concluding) volume [see this *Bulletin*, 1958, v. 33, 1200] covers authors L–Z and lists a further 7,246 titles. Although there is no analytical index to the 14,506 entries, these 2 volumes provide a most extensive survey of the publications on medical mycology and related topics. *G. C. Ainsworth*

GRUMBACH, A. & KIKUTH, W. [Edited by.] Die Infektionskrankheiten des Menschen und ihre Erreger. [**The Infective Diseases of Man and their Causative Organisms**] Vol. I, pp. 40 + 840. Vol. II, pp. 841–1702, 56 figs. 1958. Stuttgart (14a): Georg Thieme, Herdweg 63, Germany. [DM 198.–.]

In a foreword to this monumental work the editors explain that one of their chief aims has been to provide clinicians with information about the increases in the understanding of disease processes which have been achieved by the use of the special techniques elaborated for the study of the causative organisms of infective diseases in man. In spite of the title therefore the emphasis is placed on the characteristics of the parasites and only to a small extent on the clinical aspects of the diseases they produce. More than a dozen well known authorities have contributed chapters to the book.

The first 400 pages are devoted to general considerations. Host-parasite relations are reviewed with particular reference to factors which influence on the one hand the resistance of the host and on the other the pathogenicity and virulence of the parasite—for example, invasive capacity and the ability to produce exo- or endotoxins.

Next follows a section in which are described the general characters of bacteria, including their morphology, physiology, metabolism and growth requirements. The rickettsiae, viruses, bacteriophages, fungi, protozoa and helminths are dealt with along similar lines though in less detail because of lack of precise information in many cases.

The general section on epidemiology is concerned mainly with the various modes of transmission of disease —air, water, food, vectors and carrier hosts—but consideration is also given to some of the factors responsible for the rise and fall of epidemics and pandemics.

An important section is devoted to general immunology, including both active and passive immunity, with particular reference to the production of antibodies and the immunity which follows infection in some but not all diseases.

The next section deals with the theoretical basis of the rational approach to the search for chemotherapeutic remedies, and describes some of the methods used in investigating the action of drugs. The final sections in the general part describe techniques for disinfection, sterilization and the destruction of rodent carriers and insect vectors of disease.

In the second part of the work, pathogenic microorganisms and the diseases they cause are dealt with individually. In each instance the clinical picture of the disease is described first and then follow aetiology, pathogenicity, epidemiology, diagnosis, therapy and prophylaxis. Attention is focussed mainly on the aetiological agents, all the characteristics of which are described with a wealth of detail, which makes this a reference book of great value so far as these matters are concerned. The other aspects, however, are dealt with in a rather summary matter, and there are no illustrations of the microscopical appearances of either protozoa or helminths. *J. C. Broom*

Printed in Great Britain by The Eastern Press, Ltd., London and Reading.